Supplementary Information

Table s1. Factor scores of PCR used for Eq. 3

Cpd.	f_1	f_2	f_3	f_4	f_5	f_6	f_7	f_8	f_9	f_{10}	f_{11}	f_{12}	f_{13}	f_{14}
1	-1.442	-0.839	-0.275	0.486	0.415	-0.886	-0.587	0.358	-1.105	-0.361	0.074	-0.426	0.111	1.614
2	-1.102	-0.307	0.442	0.563	0.606	-0.580	-0.148	-0.633	-0.156	0.763	-2.590	-0.129	0.352	-0.441
3	-1.036	-0.072	0.334	-0.955	-0.677	-0.995	-0.032	-0.543	-0.034	0.445	-2.538	0.239	-0.565	1.639
4	-1.029	-0.803	-0.280	-0.988	-0.804	-1.415	-0.474	1.502	-0.001	0.865	-0.162	-0.151	-0.210	1.460
5	-0.969	-1.053	-0.292	-0.712	-0.644	-1.022	-0.077	1.465	-0.633	-2.269	0.012	-0.315	0.514	-1.055
6	-0.274	-1.331	-1.034	-1.078	-1.615	3.136	1.403	0.017	-0.095	0.059	1.157	-0.407	0.099	0.222
7	-0.321	-1.271	-0.611	-0.215	1.478	3.304	-0.411	-0.348	-0.688	0.732	1.467	0.095	-0.560	0.564
8	-1.253	2.051	-0.013	-1.021	1.622	-0.014	1.662	-0.296	-1.479	0.241	-0.058	-0.691	0.105	0.255
9	-1.191	1.777	0.122	1.108	-0.269	0.443	-0.699	-0.365	-2.354	-0.498	0.688	-0.545	-0.688	1.541
10	-0.751	-0.080	-0.689	1.499	-1.212	-0.130	1.933	-0.259	0.935	0.305	0.355	0.009	-0.138	-0.017
11	-0.700	-0.130	-0.731	0.640	0.362	-0.051	-1.044	-0.498	0.321	-0.548	0.428	-0.233	-0.031	-0.034
12	-0.717	-0.112	-0.608	1.116	-0.602	-0.293	-0.529	-0.067	0.370	-1.289	0.302	-0.166	-0.229	2.025
13	-1.090	-0.502	1.604	-0.604	-0.512	-0.173	-0.210	-0.510	1.017	0.668	0.258	-0.075	-0.013	0.239
14	-0.557	-0.623	-0.903	-0.709	-0.706	-0.164	-0.685	-0.131	-0.911	-1.588	0.268	-0.700	0.249	-2.783
15	-0.565	-1.285	0.364	-0.880	0.021	-0.771	-0.657	-1.505	0.994	1.243	0.086	-0.760	-0.671	-1.535
16	-0.279	-0.029	-0.849	-0.855	-0.891	-0.086	-0.498	0.080	-0.993	1.502	0.559	2.802	-0.103	-0.738
17	-0.139	-0.406	-0.512	-1.055	1.404	-0.267	-0.889	-1.186	-0.692	0.884	0.944	-0.324	-0.535	-0.689
18	-0.665	-1.284	-0.278	1.176	0.879	-0.735	2.912	-1.216	-1.157	-0.998	0.279	0.807	0.023	-0.191
19	-0.729	-0.511	-0.466	0.657	0.723	-0.844	-0.009	-0.693	-0.297	1.065	0.092	0.441	3.148	-1.199
20	-0.369	-0.341	-0.354	1.363	1.399	-0.215	-0.132	0.116	1.412	1.032	0.632	0.289	-0.340	-0.034
21	-0.769	-0.793	2.076	1.653	1.661	0.158	-0.089	1.270	1.716	0.338	0.690	-0.674	0.077	-0.233
22	-0.319	-0.022	-0.880	-1.114	-1.356	-0.400	1.295	1.239	2.471	0.455	0.278	-0.557	-0.115	-0.457
23	-0.023	0.628	-1.062	1.051	-0.752	0.139	-0.411	-0.417	2.487	-1.243	0.647	0.330	-0.449	0.865
24	0.104	-0.632	-0.310	0.224	0.213	3.041	-0.304	0.250	0.289	-0.177	-4.360	-0.174	0.065	-0.250
25	-0.887	2.715	1.755	-0.786	-0.972	0.754	1.666	0.014	0.333	0.354	0.448	-0.980	-0.038	-0.249
26	-0.504	3.288	-0.605	0.355	0.214	0.460	-0.975	0.044	0.322	0.259	-0.110	-0.593	-0.175	-1.853
27	0.101	0.476	1.411	-0.590	-0.620	0.335	-0.154	0.154	0.511	0.268	0.116	3.151	-0.063	0.524
28	0.460	0.915	-0.683	-0.676	1.159	-0.101	0.120	-0.172	0.502	-1.923	-0.255	3.712	0.055	0.064
29	0.309	-0.094	1.679	-0.711	-0.383	0.160	-0.655	-0.890	0.199	-2.608	0.208	-0.389	-0.466	-0.302
30	0.673	0.609	-0.924	0.174	0.273	-0.162	-1.536	-0.822	0.720	-1.277	-0.340	-0.654	-0.663	-0.722
31	0.652	-0.078	1.700	0.525	0.224	0.394	-0.739	2.166	-0.412	-0.107	0.169	0.262	-0.008	-0.016
32	0.963	0.575	-0.651	1.215	1.042	0.139	-0.814	2.159	0.154	0.856	0.259	0.208	-0.451	-0.478
33	1.208	-0.387	1.445	1.427	-0.711	-0.143	0.232	-0.685	-0.997	0.270	-0.010	-0.063	-1.012	0.077
34	1.500	0.421	-0.849	-1.403	1.683	-0.712	0.234	-0.915	0.603	1.159	0.036	-0.368	-0.737	1.137
35	1.667	-0.654	1.128	-0.740	-0.931	-0.400	-0.582	-1.471	-0.387	0.444	0.351	-0.481	-1.510	0.382
36	1.984	0.022	-1.078	1.278	-1.215	-0.730	-0.101	-0.863	-0.573	0.576	-0.288	-0.274	-1.385	-0.346
37	1.533	-0.716	1.571	-1.506	2.049	-0.218	0.870	1.040	-0.025	-1.437	0.194	-0.522	-0.048	0.001
38	1.890	0.206	-1.021	0.223	0.365	-0.819	2.689	1.169	-0.391	0.037	-0.862	-0.434	-0.924	-0.538
39	1.015	0.576	1.176	-0.883	-0.818	0.077	-0.353	-0.710	0.154	0.622	0.238	0.145	2.452	-0.083
40	1.453	-0.165	1.116	2.087	-1.366	0.238	0.153	-0.244	-1.001	0.381	0.096	0.274	1.759	-0.569
41	1.851	0.336	-1.287	-0.577	0.185	-0.030	-0.399	-0.350	0.394	-0.402	0.125	-1.390	3.403	2.198
42	0.319	-0.072	-0.678	-0.758	-0.919	-0.421	-0.980	2.752	-1.524	0.899	0.118	-0.291	-0.289	0.007

Table s2. Value of descriptors used for Eqs. 4-14

Cpd.	IC_2	EP_{21}	Q_{19}	FEL_2	Q_{25}	I_{25}	R_1	EP_{22}	EP_{23}	S_{11}	Q_6	Q_{11}
1	4.119	-0.004	0.574	-0.010	-0.082	0	7.249	0.133	-0.272	12.102	-0.193	-0.510
2	4.363	0.093	0.569	0.004	-0.196	1	7.253	0.071	-0.261	12.122	-0.197	-0.505
3	4.302	0.304	0.625	-0.006	-0.172	0	7.253	-0.006	-0.253	12.125	-0.188	-0.515
4	4.162	0.017	0.566	-0.007	-0.141	0	7.253	-0.062	-0.202	12.140	-0.187	-0.520
5	4.219	-0.052	0.570	0.019	0.070	0	7.253	0.144	-0.253	12.134	-0.183	-0.500
6	4.372	-0.024	0.567	0.001	-0.143	1	7.260	0.175	-0.250	12.134	-0.208	-0.471
7	4.372	0.022	0.610	-0.002	-0.001	0	7.260	0.107	-0.260	12.134	-0.188	-0.512
8	4.363	-0.061	0.616	-0.004	0.252	0	7.268	0.163	-0.270	12.099	-0.207	-0.478
9	4.363	0.039	0.588	-0.011	-0.189	0	7.268	0.091	-0.257	12.099	-0.184	-0.499
10	4.376	-0.030	0.611	0.004	-0.294	1	7.266	0.122	-0.265	12.136	-0.209	-0.477
11	4.376	-0.028	0.598	0.003	-0.001	0	7.266	0.144	-0.274	12.136	-0.170	-0.488
12	4.316	-0.052	0.568	-0.008	-0.124	0	7.268	0.113	-0.257	12.142	-0.194	-0.496
13	4.363	0.083	0.566	-0.006	-0.249	1	7.242	0.031	-0.251	12.130	-0.186	-0.514
14	4.440	-0.072	0.547	0.016	0.333	0	7.266	0.212	-0.260	12.151	-0.184	-0.498
15	4.481	0.075	0.527	-0.007	0.006	0	7.247	0.092	-0.248	12.161	-0.192	-0.516
16	4.357	-0.007	0.583	-0.006	-0.205	1	7.270	0.144	-0.244	12.162	-0.190	-0.516
17	4.478	-0.005	0.562	-0.007	-0.031	0	7.268	0.073	-0.247	12.169	-0.186	-0.518
18	4.323	-0.035	0.547	0.006	0.029	0	7.255	0.155	-0.258	12.155	-0.223	-0.492
19	4.431	-0.010	0.580	0.004	0.020	0	7.261	0.121	-0.257	12.147	-0.196	-0.509
20	4.416	-0.007	0.581	-0.002	-0.324	1	7.269	0.089	-0.247	12.168	-0.195	-0.516
21	4.361	-0.126	0.578	0.006	-0.217	1	7.246	0.095	-0.271	12.167	-0.189	-0.514
22	4.375	-0.192	0.628	-0.002	-0.307	1	7.270	0.150	-0.263	12.174	-0.200	-0.474
23	4.449	-0.058	0.589	-0.006	-0.268	1	7.285	0.109	-0.251	12.176	-0.185	-0.492
24	4.534	-0.162	0.637	-0.006	-0.214	1	7.265	0.150	-0.283	12.159	-0.241	-0.478
25	4.470	0.021	0.626	-0.003	-0.212	1	7.264	0.048	-0.271	12.126	-0.212	-0.474
26	4.524	-0.078	0.604	0.004	-0.230	1	7.287	0.151	-0.259	12.132	-0.172	-0.485
27	4.509	0.014	0.639	-0.004	-0.320	1	7.266	0.061	-0.265	12.199	-0.185	-0.512
28	4.560	-0.032	0.662	0.007	-0.344	1	7.290	0.105	-0.254	12.206	-0.183	-0.486
29	4.609	0.135	0.635	0.011	-0.262	1	7.264	0.020	-0.261	12.207	-0.194	-0.494
30	4.620	0.000	0.634	0.004	-0.255	1	7.287	0.127	-0.268	12.214	-0.169	-0.487
31	4.477	-0.019	0.664	0.005	-0.298	1	7.267	0.062	-0.289	12.238	-0.194	-0.507
32	4.490	-0.151	0.631	0.005	-0.288	1	7.291	0.187	-0.283	12.244	-0.187	-0.516
33	4.621	0.042	0.597	0.000	-0.290	1	7.270	0.066	-0.293	12.266	-0.199	-0.517
34	4.633	-0.055	0.646	-0.010	-0.269	1	7.294	0.173	-0.295	12.273	-0.197	-0.511
35	4.656	0.023	0.581	-0.005	-0.296	1	7.273	0.072	-0.292	12.291	-0.183	-0.517
36	4.668	-0.069	0.634	-0.001	-0.300	1	7.297	0.145	-0.279	12.297	-0.195	-0.516
37	4.472	-0.020	0.639	0.015	-0.295	1	7.274	0.066	-0.297	12.293	-0.195	-0.478
38	4.487	-0.136	0.651	-0.001	-0.255	1	7.297	0.200	-0.304	12.299	-0.241	-0.484
39	4.704	0.018	0.596	-0.006	-0.285	1	7.275	0.060	-0.274	12.250	-0.198	-0.513
40	4.609	0.067	0.594	0.012	-0.320	1	7.278	0.015	-0.274	12.280	-0.196	-0.509
41	4.621	-0.015	0.634	-0.018	-0.290	1	7.302	0.108	-0.266	12.286	-0.230	-0.479
42	4.302	-0.164	0.615	-0.007	-0.077	0	7.274	0.197	-0.296	12.210	-0.190	-0.519
43	4.374	-0.032	0.532	0.007	0.018	0	7.265	0.137	-0.239	12.142	-0.186	-0.518
44	4.386	0.001	0.577	0.009	-0.173	1	7.304	0.121	-0.247	12.123	-0.189	-0.491
45	4.219	-0.008	0.556	-0.007	-0.103	0	7.253	0.086	-0.251	12.134	-0.190	-0.518
46	4.162	-0.195	0.631	0.004	-0.072	0	7.253	0.170	-0.278	12.140	-0.201	-0.475
47	4.475	-0.178	0.571	-0.004	-0.067	0	7.287	0.190	-0.275	12.188	-0.187	-0.515
48	4.172	-0.245	0.574	0.018	0.083	0	7.257	0.185	-0.256	12.172	-0.185	-0.495
49	4.374	-0.082	0.642	-0.009	-0.001	0	7.277	0.138	-0.256	12.204	-0.169	-0.482
50	4.388	-0.188	0.646	0.005	-0.199	1	7.365	0.187	-0.270	12.148	-0.184	-0.491
51	4.534	-0.181	0.618	-0.003	-0.215	1	7.265	0.158	-0.293	12.159	-0.160	-0.479

Table s3. Correlation analysis of the variables used in 2D QSAR equations

	pIC_{50}	IC_2	EP_{21}	Q_{19}	FEL_2	Q_{25}	I_{25}	R_1	EP_{22}	EP_{23}	S_{11}	Q_6	Q_{11}
pIC_{50}	1.00	0.59	-0.05	0.64	0.11	-0.43	0.64	0.35	0.05	-0.50	0.55	-0.09	0.36
IC_2		1.00	0.14	0.38	-0.05	-0.47	0.63	0.35	-0.10	-0.39	0.54	-0.11	0.06
EP_{21}			1.00	0.03	-0.14	-0.26	0.15	-0.33	-0.85	0.37	-0.12	-0.14	-0.03
Q_{19}				1.00	-0.05	-0.39	0.47	0.37	-0.07	-0.49	0.36	-0.20	0.45
FEL_2					1.00	0.22	0.06	0.01	0.12	-0.03	-0.02	0.29	0.07
Q_{25}						1.00	-0.71	-0.15	0.41	0.13	-0.42	0.17	-0.04
I_{25}							1.00	0.35	-0.20	-0.27	0.39	-0.20	0.25
R_1								1.00	0.38	-0.26	0.36	0.04	0.11
EP_{22}									1.00	-0.41	0.03	0.07	0.10
EP_{23}										1.00	-0.54	0.16	-0.13
S_{11}											1.00	-0.14	-0.16
Q_6												1.00	-0.34
Q_{11}													1.00

Table s4a. Observed (Obs), calculated (Calc), residual (Res), predicted residual (Presss) and LOO predicted (Pred) activities of Eqs. 3 and 5

Cpd	Obs	Eq. 3				Eq. 5			
		Calc	Res	Presss	Pred	Calc	Res	Press	Pred
1	4.886	4.535	0.351	0.484	4.402	5.203	-0.317	-0.324	5.210
3	4.678	5.200	-0.522	-0.624	5.302	4.859	-0.181	-0.522	5.200
4	4.638	5.133	-0.495	-0.572	5.210	4.686	-0.048	0.103	4.535
5	5.699	5.616	0.083	0.096	5.603	5.771	-0.072	-0.108	5.807
6	6.027	5.789	0.238	0.260	5.767	6.564	-0.537	-0.116	6.143
7	5.495	5.516	-0.021	-0.023	5.518	5.402	0.093	0.021	5.474
10	6.886	6.076	0.810	0.884	6.002	6.262	0.624	0.400	6.486
11	6.387	5.931	0.456	0.480	5.907	6.129	0.258	0.559	5.828
12	5.284	5.392	-0.108	-0.130	5.414	5.548	-0.264	-0.232	5.516
13	5.886	5.757	0.129	0.147	5.739	5.846	0.040	0.491	5.395
14	6.076	6.315	-0.239	-0.337	6.413	6.157	-0.081	-0.023	6.099
16	5.886	6.019	-0.133	-0.145	6.031	6.431	-0.545	-0.287	6.173
17	5.469	6.106	-0.637	-0.678	6.147	5.480	-0.011	0.065	5.404
18	5.553	5.380	0.173	0.198	5.355	5.365	0.188	0.013	5.540
19	5.699	5.984	-0.285	-0.316	6.015	5.446	0.253	0.080	5.619
20	5.721	6.393	-0.672	-0.780	6.501	6.174	-0.453	-0.596	6.317
21	6.292	6.215	0.077	0.102	6.190	6.315	-0.023	0.187	6.105
23	6.569	6.827	-0.258	-0.356	6.925	6.748	-0.179	-0.013	6.582
25	6.041	6.378	-0.337	-0.527	6.568	5.903	0.138	-0.334	6.375
26	7.208	7.127	0.081	0.157	7.051	6.908	0.300	0.288	6.920
28	7.066	6.823	0.243	0.261	6.805	7.043	0.023	-0.013	7.079
29	7.229	6.570	0.659	0.687	6.542	6.446	0.783	0.701	6.528
30	7.337	7.164	0.173	0.191	7.146	7.414	-0.077	0.304	7.033
32	7.553	7.108	0.445	0.480	7.073	7.225	0.328	0.249	7.304
33	6.959	6.617	0.342	0.384	6.575	6.688	0.271	0.188	6.771
34	7.509	7.095	0.414	0.487	7.022	7.266	0.243	0.458	7.051
36	7.237	7.377	-0.140	-0.167	7.404	7.312	-0.075	-0.034	7.271
37	6.678	7.042	-0.364	-0.421	7.099	7.393	-0.715	-0.804	7.482
38	7.097	7.455	-0.358	-0.421	7.518	7.105	-0.008	-0.527	7.624
40	6.678	6.971	-0.293	-0.336	7.014	6.722	-0.044	-0.479	7.157
41	6.796	6.948	-0.152	-0.211	7.007	6.889	-0.093	-0.039	6.835
42	6.357	6.019	0.338	0.393	5.964	6.175	0.182	0.390	5.967

Table s4b. Observed (Obs), calculated (Calc), residual (Res), predicted residual (Press) and LOO predicted (Pred) activities of Eqs. 6 and 7

Cpd	Obs	Eq. 6				Eq. 7			
		Calc	Res	Press	Pred	Calc	Res	Press	Pred
1	4.886	5.136	-0.250	-0.324	5.210	4.731	0.155	0.202	4.684
3	4.678	5.141	-0.463	-0.522	5.200	4.726	-0.048	-0.117	4.795
4	4.638	4.573	0.065	0.103	4.535	4.864	-0.226	-0.280	4.918
5	5.699	5.780	-0.081	-0.108	5.807	5.651	0.048	0.068	5.631
6	6.027	6.130	-0.103	-0.116	6.143	5.868	0.159	0.173	5.854
7	5.495	5.476	0.019	0.021	5.474	5.760	-0.265	-0.313	5.808
10	6.886	6.515	0.371	0.400	6.486	6.393	0.493	0.554	6.332
11	6.387	5.890	0.497	0.559	5.828	5.973	0.414	0.456	5.931
12	5.284	5.490	-0.206	-0.232	5.516	5.602	-0.318	-0.357	5.641
13	5.886	5.540	0.346	0.491	5.395	5.435	0.451	0.548	5.338
14	6.076	6.094	-0.018	-0.023	6.099	5.974	0.102	0.214	5.862
16	5.886	6.138	-0.252	-0.287	6.173	5.781	0.105	0.113	5.773
17	5.469	5.412	0.057	0.065	5.404	5.857	-0.388	-0.482	5.951
18	5.553	5.542	0.011	0.013	5.540	5.569	-0.016	-0.018	5.571
19	5.699	5.626	0.073	0.080	5.619	5.991	-0.292	-0.324	6.023
20	5.721	6.259	-0.538	-0.596	6.317	6.177	-0.456	-0.533	6.254
21	6.292	6.149	0.143	0.187	6.105	6.445	-0.153	-0.184	6.476
23	6.569	6.581	-0.012	-0.013	6.582	6.374	0.195	0.215	6.354
25	6.041	6.341	-0.300	-0.334	6.375	6.371	-0.330	-0.354	6.395
26	7.208	6.950	0.258	0.288	6.920	6.930	0.278	0.299	6.909
28	7.066	7.077	-0.011	-0.013	7.079	7.425	-0.359	-0.442	7.508
29	7.229	6.610	0.619	0.701	6.528	6.825	0.404	0.536	6.693
30	7.337	7.058	0.279	0.304	7.033	7.175	0.162	0.180	7.157
32	7.553	7.329	0.224	0.249	7.304	7.319	0.234	0.279	7.274
33	6.959	6.797	0.162	0.188	6.771	6.769	0.190	0.226	6.733
34	7.509	7.136	0.373	0.458	7.051	7.200	0.309	0.386	7.123
36	7.237	7.267	-0.030	-0.034	7.271	7.516	-0.279	-0.323	7.560
37	6.678	7.321	-0.643	-0.804	7.482	7.058	-0.380	-0.486	7.164
38	7.097	7.529	-0.432	-0.527	7.624	7.212	-0.115	-0.141	7.238
40	6.678	7.105	-0.427	-0.479	7.157	6.896	-0.218	-0.295	6.973
41	6.796	6.824	-0.028	-0.039	6.835	6.811	-0.015	-0.021	6.817
42	6.357	6.062	0.295	0.390	5.967	6.198	0.159	0.212	6.145

Table s4c. Observed (Obs), calculated (Calc), residual (Res), predicted residual (Press) and LOO predicted (Pred) activities of Eqs. 8 and 9

Cpd	Obs	Eq. 8				Eq. 9			
		Calc	Res	Press	Pred	Calc	Res	Press	Pred
2	5.959	6.286	-0.327	-0.366	6.325	5.663	0.296	0.339	5.620
3	4.678	5.188	-0.510	-0.580	5.258	4.804	-0.126	-0.293	4.971
4	4.638	4.619	0.019	0.029	4.609	4.845	-0.207	-0.276	4.914
5	5.699	5.712	-0.013	-0.021	5.720	5.742	-0.043	-0.068	5.767
6	6.027	6.243	-0.216	-0.239	6.266	5.874	0.153	0.165	5.862
8	5.721	5.703	0.018	0.020	5.701	5.587	0.134	0.311	5.410
9	5.125	5.413	-0.288	-0.333	5.458	5.494	-0.369	-0.417	5.542
10	6.886	6.589	0.297	0.317	6.569	6.409	0.477	0.526	6.360
12	5.284	5.484	-0.200	-0.226	5.510	5.532	-0.248	-0.279	5.563
13	5.886	5.758	0.128	0.172	5.714	5.471	0.415	0.484	5.402
15	5.538	4.981	0.557	0.657	4.881	5.332	0.206	0.289	5.249
17	5.469	5.400	0.069	0.078	5.391	5.796	-0.327	-0.382	5.851
18	5.553	5.527	0.026	0.030	5.523	5.597	-0.044	-0.054	5.607
20	5.721	6.344	-0.623	-0.695	6.416	6.198	-0.477	-0.543	6.264
21	6.292	6.299	-0.007	-0.008	6.300	6.444	-0.152	-0.180	6.472
22	7.222	6.510	0.712	0.753	6.469	6.811	0.411	0.514	6.708
23	6.569	6.618	-0.049	-0.057	6.626	6.318	0.251	0.273	6.296
24	6.244	6.543	-0.299	-0.342	6.586	7.049	-0.805	-0.933	7.177
25	6.041	6.459	-0.418	-0.451	6.492	6.320	-0.279	-0.297	6.338
27	6.420	6.427	-0.007	-0.007	6.427	6.660	-0.240	-0.261	6.681
28	7.066	7.033	0.033	0.044	7.022	7.414	-0.348	-0.411	7.477
29	7.229	6.659	0.570	0.656	6.573	6.933	0.296	0.421	6.808
31	7.357	6.897	0.460	0.515	6.842	7.004	0.353	0.413	6.944
32	7.553	7.299	0.254	0.294	7.259	7.253	0.300	0.342	7.211
34	7.509	7.166	0.343	0.411	7.098	7.044	0.465	0.546	6.963
35	6.699	6.814	-0.115	-0.131	6.830	6.735	-0.036	-0.045	6.744
36	7.237	7.239	-0.002	-0.003	7.240	7.434	-0.197	-0.227	7.464
37	6.678	7.318	-0.640	-0.826	7.504	7.124	-0.446	-0.553	7.231
38	7.097	7.505	-0.408	-0.496	7.593	7.081	0.016	0.018	7.079
39	7.027	6.659	0.368	0.392	6.635	6.954	0.073	0.092	6.935
41	6.796	6.852	-0.056	-0.079	6.875	6.633	0.163	0.210	6.586
42	6.357	6.034	0.323	0.444	5.913	6.024	0.333	0.417	5.940

Table s4d. Observed (Obs), calculated (Calc), residual (Res), predicted residual (Press) and LOO predicted (Pred) activities of Eqs. 10-12

Cpd	Obs	Eq. 10				Eq. 11				Eq. 12			
		Calc	Res	Press	Pred	Calc	Res	Press	Pred	Calc	Res	Press	Pred
1	4.886	5.213	-0.327	-0.420	5.306	5.101	-0.215	-0.252	5.138	4.656	0.230	0.316	4.570
2	5.959	6.258	-0.299	-0.351	6.310	5.790	0.169	0.219	5.740	5.677	0.282	0.342	5.617
4	4.638	4.424	0.214	0.385	4.253	4.868	-0.230	-0.433	5.071	4.822	-0.184	-0.239	4.877
6	6.027	6.179	-0.152	-0.173	6.200	6.616	-0.589	-0.748	6.775	5.852	0.175	0.188	5.839
7	5.495	5.539	-0.044	-0.048	5.543	5.366	0.129	0.145	5.350	5.790	-0.295	-0.347	5.842
8	5.721	5.809	-0.088	-0.100	5.821	5.515	0.206	0.254	5.467	5.723	-0.002	-0.004	5.725
9	5.125	5.415	-0.290	-0.338	5.463	5.333	-0.208	-0.240	5.365	5.517	-0.392	-0.452	5.577
11	6.387	6.016	0.371	0.436	5.951	6.206	0.181	0.241	6.146	5.985	0.402	0.439	5.948
12	5.284	5.515	-0.231	-0.262	5.546	5.638	-0.354	-0.394	5.678	5.505	-0.221	-0.246	5.530
14	6.076	6.228	-0.152	-0.222	6.298	6.075	0.001	0.001	6.075	6.066	0.010	0.020	6.056
15	5.538	4.909	0.629	0.753	4.785	5.411	0.127	0.146	5.392	5.377	0.161	0.230	5.308
16	5.886	6.135	-0.249	-0.288	6.174	6.218	-0.332	-0.437	6.323	5.733	0.153	0.165	5.721
18	5.553	5.632	-0.079	-0.090	5.643	5.459	0.094	0.123	5.430	5.591	-0.038	-0.045	5.598
19	5.699	5.703	-0.004	-0.004	5.703	5.431	0.268	0.301	5.398	6.032	-0.333	-0.364	6.063
20	5.721	6.285	-0.564	-0.630	6.351	6.064	-0.343	-0.407	6.128	6.151	-0.430	-0.484	6.205
21	6.292	6.295	-0.003	-0.004	6.296	6.203	0.089	0.103	6.189	6.360	-0.068	-0.090	6.382
22	7.222	6.496	0.726	0.771	6.451	6.961	0.261	0.306	6.916	6.730	0.492	0.713	6.509
23	6.569	6.596	-0.027	-0.031	6.600	6.789	-0.220	-0.241	6.810	6.281	0.288	0.316	6.253
24	6.244	6.541	-0.297	-0.343	6.587	6.086	0.158	0.260	5.984	7.043	-0.799	-1.037	7.281
26	7.208	7.029	0.179	0.207	7.001	6.866	0.342	0.449	6.759	6.887	0.321	0.356	6.852
27	6.420	6.395	0.025	0.027	6.393	6.501	-0.081	-0.089	6.509	6.699	-0.279	-0.312	6.732
28	7.066	7.154	-0.088	-0.113	7.179	7.173	-0.107	-0.123	7.189	7.448	-0.382	-0.481	7.547
29	7.229	6.735	0.494	0.575	6.654	6.664	0.565	0.695	6.534	7.042	0.187	0.283	6.946
30	7.337	7.170	0.167	0.190	7.147	7.500	-0.163	-0.214	7.551	7.216	0.121	0.135	7.202
31	7.357	7.024	0.333	0.383	6.974	6.766	0.591	0.640	6.717	7.051	0.306	0.395	6.962
33	6.959	6.982	-0.023	-0.026	6.985	6.744	0.215	0.249	6.710	6.817	0.142	0.159	6.800
34	7.509	7.277	0.232	0.307	7.202	7.202	0.307	0.437	7.072	7.095	0.414	0.510	6.999
35	6.699	6.879	-0.180	-0.208	6.907	7.232	-0.533	-0.670	7.369	6.744	-0.045	-0.055	6.754
39	7.027	6.672	0.355	0.382	6.645	6.691	0.336	0.374	6.653	6.985	0.042	0.052	6.975
40	6.678	7.271	-0.593	-0.707	7.385	6.931	-0.253	-0.314	6.992	7.043	-0.365	-0.472	7.150
41	6.796	6.833	-0.037	-0.057	6.853	7.206	-0.410	-0.660	7.456	6.688	0.108	0.152	6.644

Table s4e. Observed (Obs), calculated (Calc), residual (Res), predicted residual (Press) and LOO predicted (Pred) activities of Eqs.13 and 14

Cpd	Obs	Eq. 13				Eq. 14			
		Calc	Res	Press	Pred	Calc	Res	Press	Pred
1	4.886	4.722	0.164	0.205	4.681	5.236	-0.350	-0.391	5.277
2	5.959	5.659	0.300	0.335	5.624	5.932	0.027	0.031	5.928
3	4.678	4.793	-0.115	-0.228	4.906	4.876	-0.198	-0.238	4.916
4	4.638	4.888	-0.250	-0.299	4.937	4.697	-0.059	-0.083	4.721
5	5.699	5.761	-0.062	-0.082	5.781	5.770	-0.071	-0.078	5.777
6	6.027	5.894	0.133	0.141	5.886	6.672	-0.645	-0.761	6.788
7	5.495	5.725	-0.230	-0.255	5.750	5.410	0.085	0.091	5.404
8	5.721	5.639	0.082	0.127	5.594	5.500	0.221	0.260	5.461
9	5.125	5.522	-0.397	-0.433	5.558	5.315	-0.190	-0.209	5.334
10	6.886	6.424	0.462	0.501	6.385	6.373	0.513	0.579	6.307
11	6.387	5.959	0.428	0.456	5.931	6.104	0.283	0.353	6.034
12	5.284	5.574	-0.290	-0.317	5.601	5.576	-0.292	-0.316	5.600
13	5.886	5.481	0.405	0.457	5.429	5.893	-0.007	-0.008	5.894
14	6.076	6.004	0.072	0.122	5.954	6.151	-0.075	-0.088	6.164
15	5.538	5.338	0.200	0.257	5.281	5.421	0.117	0.128	5.410
16	5.886	5.773	0.113	0.120	5.766	6.469	-0.583	-0.694	6.580
17	5.469	5.818	-0.349	-0.390	5.859	5.470	-0.001	-0.001	5.470
18	5.553	5.619	-0.066	-0.074	5.627	5.456	0.097	0.117	5.436
19	5.699	5.995	-0.296	-0.319	6.018	5.469	0.230	0.249	5.450
20	5.721	6.210	-0.489	-0.540	6.261	6.223	-0.502	-0.567	6.288
21	6.292	6.472	-0.180	-0.209	6.501	6.351	-0.059	-0.065	6.357
22	7.222	6.862	0.360	0.435	6.787	6.919	0.303	0.338	6.884
23	6.569	6.344	0.225	0.241	6.328	6.780	-0.211	-0.226	6.795
24	6.244	7.092	-0.848	-0.974	7.218	6.165	0.079	0.109	6.135
25	6.041	6.335	-0.294	-0.310	6.351	6.028	0.013	0.016	6.025
26	7.208	6.916	0.292	0.309	6.899	6.927	0.281	0.350	6.858
27	6.420	6.670	-0.250	-0.268	6.688	6.519	-0.099	-0.106	6.526
28	7.066	7.414	-0.348	-0.400	7.466	7.063	0.003	0.004	7.062
29	7.229	6.897	0.332	0.420	6.809	6.491	0.738	0.826	6.403
30	7.337	7.156	0.181	0.197	7.140	7.395	-0.058	-0.072	7.409
31	7.357	7.013	0.344	0.397	6.960	6.701	0.656	0.698	6.659
32	7.553	7.279	0.274	0.308	7.245	7.222	0.331	0.396	7.157
33	6.959	6.778	0.181	0.199	6.760	6.713	0.246	0.273	6.686
34	7.509	7.067	0.442	0.512	6.997	7.279	0.230	0.264	7.245
35	6.699	6.729	-0.030	-0.035	6.734	7.143	-0.444	-0.512	7.211
36	7.237	7.441	-0.204	-0.226	7.463	7.308	-0.071	-0.083	7.320
37	6.678	7.118	-0.440	-0.524	7.202	7.413	-0.735	-1.016	7.694
38	7.097	7.117	-0.020	-0.022	7.119	7.224	-0.127	-0.184	7.281
39	7.027	6.947	0.080	0.095	6.932	6.649	0.378	0.410	6.617
40	6.678	6.995	-0.317	-0.386	7.064	6.739	-0.061	-0.072	6.750
41	6.796	6.660	0.136	0.170	6.626	6.993	-0.197	-0.253	7.049
42	6.357	6.089	0.268	0.316	6.041	6.154	0.203	0.251	6.106

Table s5a. *t*-values and *p*-values of Eqs. 3 and 5-12

Eq. 3	Parameter	*t*-value	*p*-value	Eq. 5	Parameter	*t*-value	*p*-value	Eq. 6	Parameter	*t*-value	*p*-value
	Intercept	88.08988	0.000000		Intercept	-4.78029	0.000060		Intercept	-5.18497	0.000019
	f_1	8.15859	0.000000		I25	4.80737	0.000056		R1	5.21984	0.000017
	f_2	2.18908	0.037414		EP22	3.86627	0.000662		I25	4.95096	0.000035
	f_{14}	-3.70216	0.000968		S11	5.40998	0.000011		FEL2	3.56478	0.001382
	f_9	3.16806	0.003791		Q6	3.76823	0.000853		EP23	-3.06877	0.004851
					Q11	2.40933	0.023360				

Eq. 7	Parameter	*t*-value	*p*-value	Eq. 8	Parameter	*t*-value	*p*-value	Eq. 9	Parameter	*t*-value	*p*-value
	Intercept	-5.82567	0.000004		Intercept	-3.76134	0.000829		Intercept	-4.48179	0.000132
	IC2	6.45338	0.000001		I25	5.06904	0.000025		IC2	5.43210	0.000011
	EP21	-5.52908	0.000008		R1	3.79168	0.000766		EP21	-4.52289	0.000118
	Q19	2.49887	0.019106		EP23	-2.66271	0.012903		FEL2	3.37919	0.002302
	FEL2	3.00884	0.005760		FEL2	2.33466	0.027246		Q19	2.26703	0.031937
	Q25	-2.09400	0.046156						Q25	-2.14030	0.041881

Eq. 10	Parameter	*t*-value	*p*-value	Eq. 11	Parameter	*t*-value	*p*-value	Eq. 12	Parameter	*t*-value	*p*-value
	Intercept	-4.42185	0.000155		Intercept	-4.91615	0.000046		Intercept	-5.53135	0.000009
	I25	4.64914	0.000085		I25	3.89261	0.000652		IC2	6.26244	0.000001
	EP23	-3.71942	0.000968		S11	5.75452	0.000005		Q19	2.64987	0.013761
	R1	4.46042	0.000140		Q11	3.56120	0.001514		FEL2	3.27494	0.003091
	FEL2	3.57937	0.001386		Q6	3.87437	0.000684		EP21	-2.69223	0.012481
					EP22	1.73989	0.094178		Q25	-2.04774	0.051229

Table s5b. *t*-values and *p*-values of Eqs. 13 and 14

Eq. 13	Parameter	*t*-value	*p*-value	Eq. 14	Parameter	*t*-value	*p*-value
	Intercept	-5.55837	0.000003		Intercept	-5.28662	0.000006
	IC2	7.10315	0.000000		I25	5.72366	0.000002
	EP21	-5.26596	0.000007		S11	5.99347	0.000001
	Q19	2.66273	0.011515		EP22	3.97332	0.000326
	FEL2	4.02416	0.000281		Q6	3.83267	0.000490
	Q25	-2.88244	0.006616		Q11	2.75366	0.009179

Table s6. Dataset division of kNN-MFA statistical analysis

	Total number of compounds	Compound numbers	**pIC_{50} (M)**				
			Average	Max	Min	StdDev	Sum
Training set	8	3, 9, 12, 13, 14, 16, 19, 28	6.4261	7.5530	4.6380	0.7660	218.4880
Test set	34	1, 2, 4-8, 10, 11, 15, 17, 18, 20-27, 29-42	5.7125	7.0660	4.6780	0.7195	45.7000

Table s7. Results of Pharmacophore hypotheses generated by using the BEST method for CETP inhibitors

Hypothesis no.	Total cost	Cost difference	Error cost	rms	Correlation (*R*)	Features
1	183.70	15.30	164.15	1.04	0.78	HBA, HBA1, HY-ARO, HY, HY1
2	183.70	15.30	164.40	1.05	0.77	HBA, HBA1, HY, HY1, HY2
3	184.22	14.78	164.94	1.06	0.77	HBA, HBA1, HY, HY1, HY2
4	186.05	12.95	166.67	1.10	0.75	HBA, HBA1, HY-ARO, HY, HY1
5	186.28	12.72	167.02	1.11	0.74	HBA, HY-ARO, HY-ARO1, HY-ARO2
6	186.64	12.36	167.29	1.11	0.74	HBA, HBA1, HY-ARO, HY, HY1
7	186.83	12.17	167.50	1.12	0.74	HBA, HBA1, HY-ARO, HY-ARO1, HY
8	187.78	11.22	168.53	1.14	0.73	HBA, HBA1, HY-ARO
9	188.59	10.41	169.20	1.15	0.72	HBA, HBA1, HBA2, HY
10	188.75	10.25	169.36	1.16	0.72	HBA, HY-ARO, HY, HY1, HY2

Null cost= 199.00, Fixed cost= 160.52, Configuration=18.12, All cost units are in bits.

Table s8. Results of Pharmacophore hypotheses generated by using the FAST method for CETP inhibitors

Hypothesis no.	Total cost	Cost difference	Error cost	rms	Correlation (*R*)	Features
1	181.91	17.09	163.77	1.03	0.78	HBA, HY-ARO, HY-ARO1, HY
2	183.45	15.55	164.78	1.06	0.77	HBA, HBA1, HY, HY1
3	183.81	15.19	165.68	1.08	0.76	HBA, HBA1, HY, HY-ARO
4	184.74	14.26	166.62	1.1	0.75	HBA, HBA1, HY, HY1, HY2
5	185.06	13.94	166.93	1.11	0.75	HBA, HBA1, HY, HY1
6	185.68	13.32	167.56	1.12	0.74	HBA, HBA1, HY-ARO, HY
7	186.21	12.79	167.52	1.12	0.74	HBA, HY-ARO, HY
8	186.58	12.42	168.42	1.14	0.73	HBA, HY-ARO, HY, HY1, HY2
9	186.65	12.35	168.36	1.14	0.73	HBA, HBA1, HY-ARO, HY, HY1
10	186.71	12.29	168.57	1.14	0.73	HBA, HY, HY1, HY2, HY3

Null cost= 199.00, Fixed cost= 159.39, Configuration=16.99, All cost units are in bits.

Table s9a. Fischer's randomization test for the hypotheses 1 generated by the BEST method of conformer search

Validation	Correlation coefficient
random1	0.612
random2	0.748
random3	0.666
random4	0.671
random5	0.637
random6	0.615
random7	0.660
random8	0.000
random9	0.702
random10	0.621
random11	0.000
random12	0.000
random13	0.632
random14	0.675
random15	0.000
random16	0.619
random17	0.666
random18	0.591
random19	0.624
Average (R_r)	0.513

Table s9b. Fischer's randomization test for the hypotheses 1 and 4 generated by the FAST method of conformer search

Validation	**Correlation coefficient for hypothesis 1**	**Correlation coefficient for hypothesis 4**
random1	0.000	0.417
random2	0.588	0.543
random3	0.000	0.465
random4	0.559	0.537
random5	0.547	0.540
random6	0.653	0.620
random7	0.679	0.661
random8	0.000	0.487
random9	0.000	0.461
random10	0.000	0.462
random11	0.000	0.495
random12	0.579	0.538
random13	0.688	0.621
random14	0.000	0.508
random15	0.566	0.510
random16	0.590	0.556
random17	0.659	0.604
random18	0.000	0.402
random19	0.664	0.644
Average (R_r)	0.356	0.530