

## Supplementary Materials

# In Silico Antiprotozoal Evaluation of 1.4-Naphthoquinone Derivatives against Chagas and Leishmaniasis Diseases Using QSAR, Molecular Docking, and ADME Approaches

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**Table S1.** Antiparasitic QSAR models for chagas and leishmaniasis protozoa based on naphthoquinone derivatives obtained by the replacement method. Best models in bold.

Model	N°	Descriptors	R <sup>2</sup> <sub>train</sub>	RMSE <sub>train</sub>	R <sup>2</sup> <sub>val</sub>	RMSE <sub>val</sub>
<i>Anti-T. cruzi</i>	1	JGI8	0.41	0.78	0.53	0.78
	2	MACCSFP72 • AM_Q_AB_nCi_2_MP8_P_KA_p_MAS	0.53	0.70	0.62	0.70
	3	frag75 • MACCSFP72 • N2_B_AB_nCi_2_MP0_D_KA_e-p_MAS	0.64	0.61	0.71	0.61
	4	PubchemFP605 • K_B_AB_nCi_2_SS2_C_KA_psa-r_MAS • K_B_AB_nCi_2_SSS2_P_KA_psa-c_MAS • N2_F_AB_nCi_2_MP6_C_KA_psa_MAS	0.69	0.56	0.73	0.58
	5	D288 • MACCSFP72 • MATS5v • K_B_AB_nCi_2_DS8_T_KA_e-c_MAS • K_Q_AB_nCi_2_DS3_C_KA_e_MAS	0.72	0.53	0.71	0.58
	6	<b>frag16 • MACCSFP72 • K_Q_AB_nCi_2_SS10_T_KA_r_MAS • K_B_AB_nCi_2_DS7_C_KA_e-p_MAS • K_B_AB_nCi_2_DS2_X_KA_r-c_MAS • N2_F_AB_nCi_2_NS7_P_KA_m_MAS</b>	<b>0.76</b>	<b>0.50</b>	<b>0.82</b>	<b>0.52</b>
	7	KRFP4820 • MATS5v • K_B_AB_nCi_2_DS2_T_KA_psa-p_MAS • K_F_AB_nCi_2_DS3_T_KA_p_MAS • K_B_AB_nCi_2_NS14_A_KA_psa-c_MAS • K_B_AB_nCi_2_NS3_P_KA_psa-r_MAS • K_F_AB_nCi_2_NS5_M_KA_a_MAS	0.80	0.45	0.76	0.53
<i>Anti-L. amazonensis</i>	1	KRFPC3710	0.52	0.44	0.79	0.51
	2	KRFP2 • SdssC	0.62	0.39	0.75	0.40
	3	KRFP2 • VE3_Dt • minHBint9	0.72	0.34	0.87	0.33
	4	<b>KRFP2 • minHBint9 • IC3 • MDEC-23</b>	<b>0.77</b>	<b>0.30</b>	<b>0.84</b>	<b>0.31</b>
	5	KRFP2 • D172 • VC-5 • VR1_Dt • minHBint9	0.83	0.26	0.92	0.19
	6	KRFP2 • PubchemFP206 • KRFPC3719 • AATSC2v • E3_Dt • SHBint8	0.86	0.24	0.89	0.26
	7	KRFP2 • KRFP133 • KRFPC3440 • APC2D7_C_O • ATSC8v • minHBint9 • SD_B_AB_nCi_2_DS9_A_KA_psa-c_MAS	0.89	0.21	0.90	0.22
<i>Anti-L. infatum</i>	1	AM_B_AB_nCi_2_NS0_X_KA_a-p_MAS	0.52	0.44	0.79	0.51
	2	AATSC3c • AM_B_AB_nCi_2_NS0_X_KA_a-p_MAS	0.62	0.39	0.75	0.40
	3	PubchemFP503 • MATS3c • AM_B_AB_nCi_2_NS0_X_KA_a-p_MAS	0.72	0.34	0.87	0.33
	4	D470 • MATS3c • AM_F_AB_nCi_2_SS1_C_KA_psa_MAS • AM_Q_AB_nCi_2_NS13_X_KA_a_MAS	0.77	0.30	0.84	0.31
	5	D470 • MACCSFP159 • MATS3c • AM_B_AB_nCi_2_DS1_C_KA_psa-v_MAS • AM_Q_AB_nCi_2_NS13_X_KA_a_MAS	0.83	0.26	0.92	0.19
	6	<b>MATS3c • nHBint7 • AM_F_AB_nCi_2_NS12_T_KA_a_MAS • AM_B_AB_nCi_2_NS2_C_KA_psa-v_MAS • AM_B_AB_nCi_2_SS1_C_KA_v-c_MAS • AM_Q_AB_nCi_2_NS15_X_KA_a_MAS</b>	<b>0.72</b>	<b>0.42</b>	<b>0.71</b>	<b>0.42</b>
	7	PubchemFP503 • APC2D10_C_Cl • AATSC3c • nHBint7 • AM_B_AB_nCi_2_SS4_C_KA_psa-v_MAS • AM_F_AB_nCi_2_SS1_C_KA_c_MAS • AM_Q_AB_nCi_2_NS13_X_KA_a_MAS	0.89	0.21	0.90	0.22



**Table S2.** Toxicity QSAR models based on naphthoquinone derivatives obtained by the replacement method. Best model in bold.

N°	Descriptors	R <sup>2</sup> <sub>train</sub>	RMSE <sub>train</sub>	R <sup>2</sup> <sub>val</sub>	RMSE <sub>val</sub>
1	N2_B_AB_nCi_2_MP7_P_KA_psa-p_MAS	0.79	0.29	0.75	0.35
2	KRFPC3455 • K_B_AB_nCi_2_DS3_X_KA_a-e_MAS	0.84	0.26	0.90	0.26
3	frag14 • K_B_AB_nCi_2_DS10_C_KA_psa-c_MAS • K_B_AB_nCi_2_DS3_X_KA_a-e_MAS	0.89	0.22	0.92	0.21
4	K_B_AB_nCi_2_DS1_X_KA_a-p_MAS • K_F_AB_nCi_2_SS2_P_KA_c_MAS • N2_F_AB_nCi_2_MP4_P_KA_psa_MAS • K_Q_AB_nCi_2_NS4_A_KA_v_MAS K_B_AB_nCi_2_NS3_T_KA_psa-r_MAS • K_B_AB_nCi_2_DS7_P_KA_c-p_MAS	0.93	0.17	0.83	0.27
5	• N2_B_AB_nCi_2_MP4_P_KA_psa-p_MAS • K_B_AB_nCi_2_DS3_X_KA_a-e_MAS • K_Q_AB_nCi_2_SS14_C_KA_c_MAS	<b>0.93</b>	<b>0.16</b>	<b>0.91</b>	<b>0.23</b>
6	frag74 • K_B_AB_nCi_2_NS6_C_KA_r-c_MAS • N2_B_AB_nCi_2_NS4_C_KA_psa-c_MAS • K_B_AB_nCi_2_SS3_X_KA_psa-v_MAS • K_B_AB_nCi_2_DS1_X_KA_a-v_MAS • K_Q_AB_nCi_2_SS5_P_KA_c_MAS	0.95	0.15	0.86	0.24
7	D470 • ASP-4 • K_B_AB_nCi_2_DS5_P_KA_c-p_MAS • K_B_AB_nCi_2_DS3_X_KA_a-e_MAS • K_F_AB_nCi_2_NS13_D_KA_c_MAS • K_F_AB_nCi_2_DS3_X_KA_a_MAS • K_Q_AB_nCi_2_NS0_A_KA_psa_MAS	0.96	0.13	0.83	0.27

**Table S3.** Intercorrelation matrix of the QSAR model descriptors for anti-Chagas activity.

Descriptors	<i>a</i> <sub>1</sub>	<i>a</i> <sub>2</sub>	<i>a</i> <sub>3</sub>	<i>a</i> <sub>4</sub>	<i>a</i> <sub>5</sub>	<i>a</i> <sub>6</sub>	'VIF'
<i>a</i> <sub>1</sub>	1.000	0.256	0.080	0.077	0.024	0.007	1.096
<i>a</i> <sub>2</sub>		1.000	0.400	0.180	0.090	0.009	1.517
<i>a</i> <sub>3</sub>			1.000	0.245	0.000	0.127	1.353
<i>a</i> <sub>4</sub>				1.000	0.004	0.199	1.177
<i>a</i> <sub>5</sub>					1.000	0.092	1.049
<i>a</i> <sub>6</sub>						1.000	1.137

**Table S4.** Numerical values of the QSAR antichagas model descriptors.

ID	<i>a</i> <sub>1</sub>	<i>a</i> <sub>2</sub>	<i>a</i> <sub>3</sub>	<i>a</i> <sub>4</sub>	<i>a</i> <sub>5</sub>	<i>a</i> <sub>6</sub>
1	0	0	1.496	-0.007	-0.676	13111.508
2	0	0	-0.311	-0.111	-1.751	13835.308
3	0	0	-0.277	-0.001	-1.489	13729.559
4	0	0	-0.257	0.039	-1.063	13700.292
5	0	0	-0.761	-0.438	-2.381	13861.989
6	0	0	-0.796	-0.290	-1.908	13753.676
7	0	0	-0.800	-0.229	-1.310	13723.545
8	0	0	0.756	0.172	-1.207	13759.096
9	0	0	0.867	0.161	-0.708	13662.295
10	0	0	0.910	0.158	-0.194	13635.485
11	0	0	1.406	0.187	-1.871	13936.721
12	0	0	1.522	0.173	-1.494	13820.680
13	0	0	1.577	0.169	-1.185	13788.173
14	0	0	-0.453	0.508	-2.157	14446.252
15	0	0	-0.375	0.502	-1.847	14275.599
16	0	0	-0.328	0.503	-1.655	14228.385

17	0	0	-2.170	1.029	-2.406	15688.225
18	0	0	0.537	-0.362	-0.414	13684.902
19	0	0	0.554	-0.268	-0.388	13596.148
20	0	0	0.573	-0.228	-0.380	13571.738
21	0	0	-0.160	-0.750	-0.124	13786.813
22	0	0	-0.177	-0.616	-0.083	13686.212
23	0	0	-0.171	-0.559	-0.078	13658.503
24	0	0	-0.617	-1.153	0.173	13911.535
25	0	0	-0.675	-1.042	0.222	13796.826
26	0	0	-0.684	-0.992	0.226	13765.212
27	0	0	0.386	0.027	0.262	12938.598
28	0	0	-0.824	-0.134	-1.203	13666.712
29	0	0	-0.837	-0.029	-0.992	13561.939
30	0	0	-0.834	0.011	-0.615	13532.849
31	0	0	-1.119	-0.516	-1.748	13693.570
32	0	0	-1.190	-0.383	-1.348	13586.263
33	0	0	-1.206	-0.325	-0.809	13556.318
34	0	0	-0.051	0.210	-0.502	13589.988
35	0	0	0.006	0.198	-0.041	13494.075
36	0	0	0.031	0.195	0.447	13467.411
37	0	0	0.399	0.226	-1.225	13768.792
38	0	0	0.430	0.210	-0.912	13653.665
39	0	0	0.450	0.206	-0.652	13621.316
40	0	0	-1.106	0.552	-1.604	14281.758
41	0	0	-1.158	0.544	-0.490	14854.082
42	0	0	-1.122	0.546	-0.485	14788.235
43	0	0	-2.443	1.080	-2.104	15533.840
44	0	0	-0.754	-0.657	0.917	13490.723
45	0	0	-1.014	-1.228	1.149	13743.456
46	0	0	-1.095	-1.149	1.237	13629.827
47	0	0	-1.115	-1.112	1.240	13598.431
48	0	0	-0.227	-0.385	0.516	13515.299
49	0	0	-0.239	-0.301	0.581	13427.421
50	0	0	-0.234	-0.264	0.593	13403.152
51	0	0	-0.705	-0.816	0.831	13617.895
52	0	0	-0.748	-0.705	0.912	13518.258
53	0	0	-0.216	3.325	-2.585	20485.618
54	1	0	-0.134	3.533	-2.015	20267.303
55	0	0	-0.665	1.494	-2.437	20512.441
56	1	0	-0.648	1.627	-1.595	20288.806
57	0	0	0.457	2.850	-1.153	20319.540

58	0	0	0.465	2.938	-1.131	20139.368
59	0	0	-0.127	1.110	-0.972	20426.307
60	0	0	-0.131	1.144	-0.887	20221.951
61	0	0	-0.547	0.097	-0.744	20553.937
62	0	0	-0.579	0.087	-0.630	20321.568
63	0	0	1.230	0.132	-1.352	13901.892
64	0	0	0.031	0.277	-0.683	14422.467
65	0	0	0.005	0.264	-0.948	14457.586
66	0	0	-0.050	0.265	-1.198	14584.850
67	0	0	-0.688	0.416	-1.389	15094.040
68	0	0	-0.690	0.417	-0.926	15158.033
69	2	1	-1.337	-1.666	-0.286	10706.019
70	1	1	-2.210	-1.450	-1.319	10837.766
71	1	1	-2.210	-1.811	-0.557	9985.253
72	0	0	5.295	0.680	-0.040	15172.831
73	0	0	0.560	0.585	-0.525	15775.276
74	1	1	-2.123	-1.801	-2.615	11065.610
75	1	1	-1.482	-1.523	-2.558	15667.925
76	1	1	-1.418	-1.567	-2.209	16199.941
77	1	1	-1.467	-1.538	-2.508	15933.594
78	1	1	-1.085	-1.240	-1.257	15337.065
79	1	1	-1.338	-1.235	-0.796	15870.217
80	1	1	-1.628	-1.120	-0.232	15932.004
81	1	1	-1.854	-1.163	-1.607	17108.500
82	1	1	-1.285	-1.229	-1.083	15801.566
83	1	1	-1.251	-1.402	-0.200	15582.794
84	1	1	-1.216	-1.416	-1.295	14542.430
85	1	1	-1.928	-1.222	0.102	15774.963
86	1	1	-1.769	-1.373	-0.661	15476.202
87	1	1	-1.588	-1.499	-0.885	11034.161
88	1	1	-1.729	-1.340	-1.021	15081.080
89	1	1	-1.761	-1.364	-0.649	15460.264
90	1	1	-1.572	-1.611	-0.173	11035.114
91	1	1	-1.239	-1.539	-0.665	11033.694
92	1	1	-1.162	-1.363	0.135	11036.211
93	1	1	-2.009	-1.631	-0.134	11056.678
94	1	1	-1.828	-1.621	-0.826	11132.035
95	1	1	-1.174	-1.287	2.537	15406.068
96	1	1	-1.349	-1.300	1.437	16555.827
97	1	1	-1.328	-1.300	3.314	15937.317
98	1	1	-1.574	-1.159	1.385	15998.861

99	2	1	-1.328	-1.593	-1.832	15103.452
100	0	0	2.836	-1.435	-3.039	13343.651
101	0	0	0.673	-1.176	-2.095	16440.801
102	2	0	1.448	-1.213	-1.959	14200.882
103	2	0	0.196	-0.981	-1.417	17354.751
104	2	0	1.158	-1.676	-0.606	14363.506
105	2	0	1.126	-1.524	-2.038	14563.279
106	2	0	0.918	-1.783	-1.945	14734.934
107	2	0	1.061	-1.624	-1.454	14395.389
108	2	0	0.878	-1.862	-1.182	14557.470
109	0	0	1.442	-1.550	-1.408	14630.723
110	0	1	0.628	-1.569	-2.776	15817.688
111	0	0	2.250	-1.785	-2.989	14185.373
112	0	0	1.769	-1.215	-1.270	14161.017
113	0	0	0.889	-1.183	-1.502	15416.855
114	0	0	2.519	-1.122	-2.479	14058.657
115	0	0	2.356	-0.933	-1.718	14824.455
116	0	0	2.745	-0.960	-2.058	14082.609
117	0	0	3.539	-1.340	-0.555	11369.578
118	0	0	2.226	-0.426	0.455	17529.511
119	0	0	-1.293	-1.502	-3.668	12199.662
120	0	0	3.830	-1.344	1.362	14739.716
121	0	0	1.244	-1.362	1.305	18265.655
122	1	1	-0.552	-1.466	-1.541	13016.675
123	1	1	-0.579	-1.376	-2.060	13694.258
124	1	1	-0.887	-1.482	-1.176	13478.120
125	1	1	-1.266	-1.341	-1.736	13606.876
126	1	1	-0.746	-1.367	-1.607	13541.772
127	1	1	-1.475	-1.348	-3.166	13630.209
128	1	1	-0.924	-1.659	-0.872	13189.645
129	1	1	-1.122	-1.595	-0.806	14090.598
130	2	1	0.186	-0.904	0.545	15680.558
131	1	1	-1.191	-1.795	-2.590	10924.157
132	1	1	-1.236	-1.725	-2.104	10923.306
133	1	1	-1.535	-1.583	-2.508	10917.311
134	1	1	-1.338	-1.246	-3.444	10918.804
135	1	1	-1.375	-1.332	-0.648	10918.804
136	0	1	-1.605	-1.744	-4.112	9628.535
137	0	0	1.714	-1.370	-4.420	10616.460
138	1	1	-1.832	-1.702	-1.253	10694.968
139	1	1	-1.793	-1.729	1.290	10704.129

140	1	1	-1.850	-1.765	-1.108	10696.301
141	1	1	-1.571	-1.504	0.497	10704.128
142	0	0	-1.078	-0.798	-2.488	10614.837
143	0	0	5.295	0.680	-0.040	15172.831
144	0	0	0.560	0.585	-0.525	15775.276
145	0	0	3.433	0.920	0.060	16341.484
146	0	0	-0.412	1.419	-1.550	16286.350
147	0	0	3.087	0.295	0.245	15643.198
148	0	0	-1.306	-0.461	-2.751	11247.069
149	0	0	-1.896	-1.433	-1.484	11361.414
150	0	0	-1.900	-0.796	-2.378	11540.710
151	0	0	-0.977	-0.673	-2.363	10995.990
152	0	0	4.896	0.774	-0.722	15497.619
153	0	1	-1.711	-1.168	-2.643	14895.553
154	0	1	-1.603	-1.166	0.327	15554.030
155	0	1	-2.250	-1.086	-2.702	15498.627
156	0	1	-1.871	-1.067	-0.085	14961.358
157	0	1	-1.671	-1.182	-2.905	14822.476
158	0	1	-1.085	-2.009	0.285	10067.953
159	1	1	-1.788	-1.717	-1.809	11666.624
160	1	1	-1.774	-1.571	-1.923	11564.100
161	1	1	-1.085	-1.240	-1.257	15337.065
162	1	1	-1.585	-1.752	-2.040	11710.334
163	1	1	-1.604	-1.476	-0.226	11586.318
164	1	1	-1.725	-1.828	-1.079	11015.382
165	1	1	-1.471	-1.561	0.188	14047.617
166	1	1	-1.269	-1.497	-0.434	13688.571
167	1	1	-1.229	-1.494	0.510	14125.127
168	1	1	-1.849	-1.344	-1.350	14141.500
169	1	1	-1.289	-1.497	-0.078	13660.717
170	1	1	-1.247	-1.495	0.720	14083.651
171	1	1	-1.857	-1.347	-1.217	14101.207
172	1	1	-1.611	-1.444	0.562	13575.192
173	1	1	-1.341	-1.500	1.058	13510.718
174	1	1	-1.566	-1.496	0.845	12774.773
175	0	0	1.551	-1.669	-3.294	10249.534
176	0	0	0.001	-1.960	-0.558	10426.094
177	1	1	-0.153	-1.383	-2.847	10458.401
178	1	1	-1.553	-1.267	-5.268	10533.181
179	0	0	1.268	-1.358	-3.523	10980.540
180	0	0	1.404	-1.165	-3.005	11000.013



181	0	0	-0.295	-1.424	-3.171	11310.044
182	0	0	-1.437	-1.534	-5.069	11728.993
183	0	0	-1.030	-1.670	-3.440	11481.003
184	0	0	-0.126	-1.131	-2.126	12033.028
185	0	0	-1.437	-1.151	-3.979	12446.730
186	0	0	-0.906	-1.340	-2.824	12202.023
187	0	0	-0.161	-1.135	-2.160	12043.199
188	0	0	-1.444	-1.190	-3.943	12459.355
189	0	0	-0.933	-1.349	-2.754	12213.320
190	0	0	-0.922	-1.817	-1.026	11483.303
191	3	1	-1.851	-1.714	-2.089	11954.476
192	3	1	-1.960	-1.766	-0.125	11814.965
193	3	1	-0.910	-1.259	-1.113	14950.935
194	3	1	-0.897	-1.289	-0.690	14787.511
195	3	1	-0.904	-1.258	-2.242	14546.030
196	3	1	-1.144	-1.386	-2.334	14342.728
197	3	1	-1.197	-1.407	-0.561	14173.887
198	3	1	-1.448	-1.235	-1.585	14463.791
199	3	1	-0.917	-1.355	-2.625	13909.987
200	3	1	-0.965	-1.380	-0.816	13736.730
201	3	1	-1.166	-1.569	-1.981	14073.395
202	1	1	-1.412	-1.423	0.441	13878.897
203	1	1	2.508	-1.418	0.071	14357.454
204	1	1	-1.587	-1.428	1.706	13299.283
205	1	1	-1.391	-1.416	0.202	13920.235
206	1	1	-1.503	-1.420	-0.275	13478.794
207	1	1	-1.581	-1.426	0.930	13322.109
208	1	1	-0.928	-1.293	-0.013	16516.650
209	1	1	-1.180	-1.209	-0.132	16624.801
210	2	1	-1.309	-1.946	-1.200	10699.968
211	1	1	-1.067	-1.761	1.966	10974.098
212	1	1	-1.546	-1.866	-1.893	11391.144
213	1	1	-1.503	-1.826	-2.421	11457.450
214	1	1	-1.758	-1.677	-3.289	11396.658
215	1	1	-1.499	-1.913	-1.727	11618.522
216	1	1	-1.531	-1.699	-1.846	11329.871
217	0	1	-1.226	-1.767	3.056	13595.912
218	1	1	3.308	-1.173	1.527	17325.021
219	2	1	-1.512	-1.700	-1.098	10744.198
220	1	1	-1.374	-1.948	-2.318	10507.910
221	2	1	-1.309	-1.946	-1.200	10699.968

**Table S5.** Experimental and predicted values of antichagas activity. Residuals and influence values  $h$  ( $h^{\text{lim}} = 0.196$ ) are reported. ^ validation group and \* test group.

ID	Experimental activity	Predicted activity	Residuals	$h$
69	2.614	2.913	-0.300	0.034
70	2.503	2.618	-0.116	0.019
71	2.254	2.582	-0.328	0.026
72	1.037	1.819	-0.781	0.183
73^	1.661	2.000	-0.339	0.113
74^	1.701	1.986	-0.285	0.028
75	1.907	1.347	0.561	0.024
76^	0.833	1.268	-0.436	0.021
77	0.914	1.292	-0.378	0.023
78	1.238	1.887	-0.649	0.020
79	1.318	1.907	-0.589	0.023
80*	2.555	2.143	0.413	0.032
81	1.338	1.642	-0.304	0.037
82^	1.598	1.865	-0.268	0.022
83	1.396	1.909	-0.512	0.022
84	1.641	1.872	-0.231	0.016
85	1.775	2.170	-0.395	0.036
86	2.454	1.919	0.535	0.023
87	2.721	2.557	0.164	0.015
88*	1.745	1.950	-0.205	0.021
89^	2.194	1.932	0.262	0.023
90	2.429	2.587	-0.159	0.020
91	1.674	2.526	-0.852	0.017
92	2.747	2.839	-0.092	0.019
93	2.395	2.615	-0.220	0.022
94	1.369	2.459	-1.090	0.017
95*	2.496	2.570	-0.074	0.073
96^	2.643	2.152	0.491	0.052
97	2.342	2.625	-0.283	0.105
98	2.026	2.400	-0.374	0.052
99	2.368	1.873	0.495	0.028
100	-0.229	-0.173	-0.056	0.086
101	-0.658	-0.100	-0.558	0.043
102	1.623	0.954	0.669	0.085
103	1.394	0.822	0.572	0.103
104	-0.004	0.777	-0.781	0.110
105	0.549	0.611	-0.062	0.091

106	0.879	0.373	0.506	0.101
107^	0.130	0.666	-0.536	0.097
108*	0.609	0.483	0.126	0.112
109*	0.068	-0.064	0.132	0.055
110	0.210	0.658	-0.449	0.080
111	-0.310	-0.590	0.280	0.084
112^	-0.252	0.333	-0.584	0.045
113	0.207	0.175	0.031	0.040
114	0.140	0.131	0.009	0.059
115	0.352	0.331	0.021	0.048
116	0.861	0.337	0.524	0.059
117^	0.253	0.689	-0.436	0.114
118	0.093	0.743	-0.650	0.074
119	0.780	0.268	0.512	0.065
120^	-0.721	0.405	-1.126	0.155
121	0.342	-0.014	0.356	0.115
122	1.748	1.992	-0.244	0.021
123	1.305	1.855	-0.550	0.024
124	1.711	1.996	-0.286	0.016
125*	2.084	2.036	0.048	0.018
126	1.989	1.995	-0.006	0.019
127	2.121	1.770	0.351	0.036
128^	2.090	1.945	0.145	0.018
129*	2.837	1.872	0.966	0.016
130	2.929	2.724	0.205	0.051
131	1.797	1.929	-0.132	0.031
132*	2.207	2.094	0.113	0.025
133^	1.549	2.181	-0.632	0.026
134	2.520	2.299	0.221	0.048
135	2.945	2.760	0.184	0.015
136	2.593	1.600	0.993	0.084
137	1.090	0.238	0.852	0.078
138	2.558	2.382	0.176	0.019
139*	2.598	2.841	-0.243	0.045
140	2.568	2.351	0.217	0.020
141	2.313	2.878	-0.565	0.024
142	1.619	1.431	0.188	0.042
143^	1.037	1.819	-0.781	0.183
144	1.661	2.000	-0.339	0.113
145	2.692	2.036	0.656	0.143
146	3.302	2.593	0.710	0.264

147*	2.053	1.645	0.409	0.090
148	1.248	1.604	-0.356	0.063
149	1.904	0.969	0.935	0.077
150	1.830	1.365	0.465	0.073
151	1.714	1.492	0.222	0.043
152	1.623	1.756	-0.133	0.175
153	1.318	1.468	-0.150	0.060
154^	2.006	1.910	0.096	0.059
155	1.338	1.476	-0.138	0.073
156	2.555	2.061	0.495	0.057
157*	1.598	1.413	0.184	0.062
158	3.107	2.065	1.043	0.070
159	2.182	2.076	0.105	0.019
160	2.542	2.210	0.332	0.019
161*	1.238	1.887	-0.649	0.020
162	1.762	1.970	-0.208	0.021
163	2.409	2.605	-0.196	0.017
164	2.327	2.226	0.101	0.021
165	3.245	2.138	1.106	0.024
166	2.522	2.125	0.397	0.017
167	2.149	2.225	-0.076	0.026
168	1.936	2.068	-0.132	0.020
169*	2.585	2.200	0.384	0.019
170*	2.979	2.274	0.705	0.030
171^	2.933	2.098	0.835	0.020
172	1.945	2.422	-0.477	0.028
173*	3.401	2.450	0.951	0.035
174*	2.534	2.570	-0.036	0.031
175	-0.102	0.257	-0.359	0.071
176	0.781	0.632	0.149	0.083
177	2.751	2.250	0.501	0.053
178	1.799	2.019	-0.220	0.104
179	0.137	0.400	-0.263	0.050
180	0.336	0.664	-0.328	0.040
181^	0.814	0.501	0.313	0.041
182	-0.796	0.069	-0.865	0.088
183	0.009	0.259	-0.250	0.060
184	0.332	0.829	-0.496	0.030
185^	0.386	0.508	-0.123	0.071
186*	0.097	0.544	-0.447	0.048
187*	0.401	0.820	-0.419	0.031

188	-0.071	0.476	-0.547	0.071
189	0.149	0.550	-0.401	0.048
190	0.140	0.575	-0.435	0.075
191*	3.335	2.706	0.629	0.083
192	3.231	3.073	0.158	0.086
193	2.340	2.678	-0.338	0.079
194	3.569	2.760	0.810	0.078
195	1.430	2.535	-1.105	0.088
196	1.371	2.457	-1.086	0.085
197^	3.448	2.816	0.632	0.077
198	3.521	2.752	0.768	0.084
199	3.225	2.488	0.737	0.091
200*	3.260	2.850	0.410	0.077
201*	2.916	2.405	0.511	0.078
202	2.960	2.343	0.617	0.025
203*	2.573	1.794	0.779	0.119
204	3.168	2.706	0.462	0.048
205^	3.039	2.293	0.746	0.022
206*	2.644	2.290	0.354	0.018
207^	1.951	2.554	-0.603	0.033
208	2.896	1.843	1.053	0.026
209^	2.362	1.904	0.458	0.028
210	2.547	2.472	0.075	0.039
211	2.600	2.818	-0.218	0.062
212	2.329	1.946	0.383	0.023
213	1.952	1.866	0.086	0.026
214	1.723	1.875	-0.152	0.036
215^	1.743	1.887	-0.144	0.023
216	1.938	2.123	-0.185	0.020
217	2.052	2.192	-0.140	0.127
218	2.097	1.680	0.417	0.163
219	2.217	2.736	-0.519	0.031
220	2.624	1.932	0.692	0.032
221^	2.519	2.472	0.048	0.039

**Table S6.** Values predicted by the QSAR model of anti-Chagas activity of the 68 naphthoquinone derivatives (prediction group).

ID	Predicted activity	$h^* = 0.196$
1	1.808	0.041
2	1.551	0.064
3	1.721	0.068
4	1.844	0.069
5	1.161	0.063
6	1.415	0.068
7	1.594	0.070
8	1.830	0.059
9	1.922	0.055
10	2.020	0.056
11	1.618	0.061
12	1.687	0.056
13	1.743	0.054
14	1.959	0.126
15	2.036	0.118
16	2.078	0.115
17	2.346	0.299
18	1.515	0.040
19	1.623	0.042
20	1.664	0.043
21	1.255	0.051
22	1.409	0.052
23	1.469	0.052
24	0.955	0.072
25	1.096	0.072
26	1.150	0.071
27	2.164	0.055
28	1.717	0.076
29	1.878	0.081
30	1.993	0.085
31	1.276	0.068
32	1.506	0.076
33	1.672	0.081
34	2.113	0.074
35	2.203	0.074
36	2.297	0.078
37	1.911	0.067

38	1.975	0.064
39	2.025	0.064
40	2.203	0.149
41	2.309	0.157
42	2.321	0.155
43	2.508	0.319
44	1.658	0.084
45	1.143	0.109
46	1.264	0.111
47	1.306	0.111
48	1.78	0.064
49	1.889	0.067
50	1.93	0.067
51	1.463	0.082
52	1.605	0.084
53	3.399	0.810
54	4.101	0.871
55	1.739	0.375
56	2.430	0.400
57	3.189	0.598
58	3.309	0.616
59	1.621	0.268
60	1.707	0.270
61	0.727	0.169
62	0.785	0.167
63	1.690	0.054
64	1.981	0.085
65	1.913	0.085
66	1.848	0.088
67	1.924	0.127
68	2.003	0.128

**Table S7.** Intercorrelation matrix of the QSAR model descriptors for antileishmanial activity.

QSAR model for anti- <i>L. amazonensis</i>							
Descriptor	$b_1$	$b_2$	$b_3$	$b_4$	VIF		
$b_1$	1	0.00277	0.02	0.14	1.04		
$b_2$		1	0.000131	0.14	1.05		
$b_3$			1	0.19	1.05		
$b_4$				1	1.25		
QSAR model for anti- <i>L. infantum</i>							
Descriptor	$c_1$	$c_2$	$c_3$	$c_4$	$c_5$	$c_6$	VIF
$c_1$	1	0.01	0.02	0.03	0.03	0.01	1.00
$c_2$		1	0.03	0.04	0.09	0.03	1.03
$c_3$			1	0.27	0.21	0.15	1.45
$c_4$				1	0.79	0.05	3.34
$c_5$					1	0.04	2.87
$c_6$						1	1.25

**Table S8.** Numerical values of the QSAR anti-*L. amazonensis* model descriptors.

ID	$b_1$	$b_2$	$b_3$	$b_4$
1	0	0	4.12	16.79
2	0	0	4.54	17.05
3	0	0	4.63	17.61
4	0	0	4.48	17.99
5	0	0	4.65	18.55
6	0	0	4.74	18.8
7	0	0	4.59	18.9
8	0	0	4.37	17.05
9	0	0	4.48	17.61
10	0	0	4.37	17.99
11	0	0	4.37	17.05
12	0	0	4.48	17.61
13	0	0	4.37	17.99
14	0	0	4.44	17.05
15	0	0	4.6	17.61
16	0	0	4.38	17.99
17	0	0	4.68	17.37
18	0	0	4.42	17.05
19	0	0	4.57	17.61
20	0	0	4.35	17.99
21	0	0	4.54	19.11
22	0	0	4.68	19.29
23	0	0	4.54	19.34



24	0	0	4.43	18.65
25	0	0	4.56	19.19
26	0	0	4.43	19.52
27	0	0	4.07	16.79
28	0	0	4.48	17.05
29	0	0	4.57	17.61
30	0	0	4.43	17.99
31	0	0	4.6	18.55
32	0	0	4.68	18.8
33	0	0	4.55	18.9
34	0	0	4.31	17.05
35	0	0	4.41	17.61
36	0	0	4.31	17.99
37	0	0	4.31	17.05
38	0	0	4.41	17.61
39	0	0	4.31	17.99
40	0	0	4.38	17.05
41	0	0	4.54	17.61
42	0	6.02	4.32	17.99
43	0	6.36	4.61	17.37
44	0	0	4.49	19.34
45	0	0	4.39	18.65
46	0	0	4.52	19.19
47	0	0	4.39	19.52
48	0	0	4.36	17.05
49	0	0	4.51	17.61
50	0	0	4.31	17.99
51	0	0	4.49	19.11
52	0	0	4.63	19.29
53	0	0	4.27	17.21
54	0	0	4.29	18.03
55	0	0	4.4	18.96
56	0	0	4.42	19.36
57	0	0	4.13	17.21
58	0	0	4.22	18.03
59	0	0	4.34	19.6
60	0	0	4.36	19.93
61	0	0	4.23	18.48
62	0	0	4.25	19.33
63	0	0	4.63	18.37
64	0	5.15	4.82	19.85

65	0	0	4.91	19.65
66	0	0	4.82	19.33
67	0	5.32	4.93	20.04
68	0	5.36	4.98	20.02
222	0	0	4.26	21.34
223	0	0	4.37	18.94
224	0	0	4.19	15.2
225	0	0	4.15	15.2
69	0	0	4.14	14.32
226	0	0	4.93	20.93
227	0	0	4.96	19.47
228	0	0	5	20.76
229	0	0	3.79	4.75
230	0	0	3.69	4.75
231	0	0	3.75	6.45
232	0	0	4.21	9.82
233	0	0	4.16	12.3
234	1	0	4.61	26.8
235	1	0	4.67	23.65
236	1	0	4.84	23.5
237	1	0	4.88	24.57
238	1	0	4.95	27.33
239	1	0	4.95	26.92
240	1	0	4.67	23.69
241	0	0	5.01	26.03
242	0	0	5.16	25.39
243	0	0	5.16	25.52
244	0	0	5.05	24.26
245	0	0	5.18	21.58
246	0	0	5.12	23.06
247	0	0	3.17	11.11
248	0	0	1.92	5.66
249	0	0	3.83	11.11
250	0	0	3.32	10.48
251	0	0	3.97	9.35
252	0	0	4.57	10.14
253	0	0	4.47	15.81
254	0	0	4.79	14.18
255	0	0	4.77	14.18
256	0	0	4.98	15.66
257	0	0	4.98	15.66

258	0	0	4.67	15.66
259	0	0	4.6	15.66
260	0	0	5.02	16.61
261	0	0	3.9	25.71
262	0	0	4.44	34.38
263	1	0	4.28	31.45
264	0	0	4.19	39.51
265	0	6.8	4.44	39.7
266	0	3.8	4.5	39.7
267	0	0	4.39	39.7
268	0	0	4.9	21.29
269	0	0	4.81	21.29
270	0	0	5.05	15.3
271	0	0	4.92	21.31
272	0	0	4.47	6.98
273	0	0	3.94	5.14
274	0	0	4.18	7.38
275	0	0	4.64	9.07
276	0	0	4.05	7.38
277	0	0	3.83	5.14
278	0	0	4.05	7.38
279	0	0.39	4.47	11.45
280	0	0	4.53	11.8

**Table S9.** Numerical values of the QSAR anti-*L. infantum* model descriptors.

ID	$c_1$	$c_2$	$c_3$	$c_4$	$c_5$	$c_6$
1	0.06	0	-3.44E+05	58.58	0.43	-6.95E+04
2	0.19	0	-3.47E+05	53.25	0.25	-1.19E+04
3	0.01	0	-3.42E+05	53.25	0.25	-2.34E+04
4	0.04	0	-3.41E+05	53.25	0.25	-2.65E+04
5	0.16	0	-3.35E+05	55.44	0.48	-9.55E+03
6	-0.02	0	-3.29E+05	55.44	0.48	-2.12E+04
7	0.02	0	-3.28E+05	55.44	0.48	-2.40E+04
8	0.16	0	-3.34E+05	55.79	0.41	-1.25E+05
9	-0.01	0	-3.33E+05	55.79	0.41	-1.19E+05
10	0.04	0	-3.33E+05	55.79	0.41	-1.17E+05
11	0.14	0	-3.24E+05	55.79	0.41	-2.00E+05
12	0.01	0	-3.25E+05	55.79	0.41	-1.82E+05
13	0.05	0	-3.26E+05	55.79	0.41	-1.77E+05
14	0.08	0	-3.64E+05	50.94	0.38	1.15E+05
15	0.01	0	-3.56E+05	50.94	0.37	5.74E+04
16	0.06	0	-3.54E+05	50.94	0.37	5.08E+04
17	0.07	0	-3.79E+05	45.06	0.33	2.71E+05
18	0.09	0	-3.58E+05	55.79	0.41	-5.00E+04
19	0.04	0	-3.53E+05	55.79	0.4	-5.84E+04
20	0.05	0	-3.52E+05	55.79	0.4	-5.87E+04
21	0.09	0	-3.48E+05	53.25	0.42	-4.61E+04
22	0.05	0	-3.43E+05	53.25	0.42	-5.39E+04
23	0.05	0	-3.42E+05	53.25	0.42	-5.49E+04
24	0.07	0	-3.48E+05	50.94	0.42	-4.02E+04
25	0.04	0	-3.41E+05	50.94	0.42	-4.79E+04
26	0.05	0	-3.39E+05	50.94	0.42	-4.96E+04
27	0.16	0	-3.97E+05	102.39	0.38	3.73E+05
28	0.25	0	-3.96E+05	93.08	0.2	4.01E+05
29	0.1	1	-3.90E+05	93.08	0.2	3.84E+05
30	0.13	0	-3.89E+05	93.08	0.2	3.79E+05
31	0.22	0	-3.81E+05	93.54	0.43	3.85E+05
32	0.07	1	-3.76E+05	93.54	0.43	3.68E+05
33	0.1	0	-3.74E+05	93.54	0.43	3.64E+05
34	0.23	0	-3.85E+05	97.51	0.36	2.88E+05
35	0.09	1	-3.84E+05	97.51	0.36	2.96E+05
36	0.13	0	-3.84E+05	97.51	0.36	2.99E+05
37	0.23	0	-3.75E+05	97.51	0.36	2.03E+05
38	0.12	1	-3.76E+05	97.51	0.36	2.27E+05
39	0.15	0	-3.77E+05	97.51	0.36	2.34E+05

40	0.17	1	-4.12E+05	89.03	0.33	5.13E+05
41	0.11	0	-4.03E+05	89.03	0.33	4.57E+05
42	0.15	0	-4.00E+05	89.03	0.33	4.43E+05
43	0.15	1	-4.21E+05	78.76	0.29	6.30E+05
44	0.16	0	-3.90E+05	93.08	0.37	3.49E+05
45	0.17	0	-3.95E+05	89.03	0.38	3.56E+05
46	0.14	0	-3.87E+05	89.03	0.38	3.42E+05
47	0.15	0	-3.85E+05	89.03	0.38	3.38E+05
48	0.19	0	-4.09E+05	97.51	0.36	3.77E+05
49	0.15	0	-4.04E+05	97.51	0.35	3.67E+05
50	0.16	0	-4.02E+05	97.51	0.35	3.64E+05
51	0.18	0	-3.97E+05	93.08	0.38	3.63E+05
52	0.15	0	-3.92E+05	93.08	0.37	3.52E+05
53	0.11	0	-4.96E+05	13.15	-0.02	-2.47E+05
54	-2.23E-03	0	-4.87E+05	13.15	-0.02	-2.51E+05
55	0.08	0	-4.77E+05	17.09	0.22	-2.37E+05
56	-0.02	0	-4.68E+05	17.09	0.22	-2.40E+05
57	0.08	0	-5.12E+05	13.78	0.13	-3.10E+05
58	0.04	0	-5.05E+05	13.78	0.12	-3.01E+05
59	0.07	0	-4.96E+05	13.15	0.16	-2.98E+05
60	0.05	0	-4.88E+05	13.15	0.15	-2.88E+05
61	0.06	0	-4.91E+05	12.58	0.17	-2.95E+05
62	0.04	0	-4.80E+05	12.58	0.16	-2.82E+05
63	0.08	0	-3.43E+05	50.62	0.35	4.42E+03
64	0.07	0	-3.35E+05	48.75	0.33	-4.26E+04
65	0.03	0	-3.35E+05	48.75	0.33	-4.51E+04
66	0.12	1	-3.37E+05	48.75	0.33	-5.14E+04
67	0.06	0	-3.26E+05	47.01	0.32	-9.51E+04
68	0.04	1	-3.28E+05	47.01	0.32	-9.56E+04
281	-0.06	0	-2.84E+05	69.68	0.52	-3.13E+05
282	-0.01	0	-3.28E+05	80.16	0.32	1.01E+05
283	-0.06	0	-4.03E+05	72.99	0.45	3.40E+04
284	-0.08	0	-3.64E+05	69.68	0.55	-2.95E+05
285	0	0	-3.96E+05	100.64	0.58	3.80E+04
286	0.07	0	-2.72E+05	80.79	0.47	2.48E+04
222	-0.04	0	-2.42E+05	66.83	0.34	2.49E+04
223	-2.75E-04	0	-3.36E+05	44.39	-0.04	2.22E+04
287	0.02	0	-3.19E+05	64.19	0.34	2.98E+04
288	-0.02	0	-3.16E+05	84.24	0.33	8.64E+03
224	-9.44E-04	0	-3.05E+05	53.74	0.09	2.39E+04
225	0.03	0	-3.10E+05	49.91	0.21	2.35E+04

289	0.03	0	-3.72E+05	83.68	0.3	1.52E+05
69	4.68E-03	0	-3.23E+05	80.43	0.29	3.38E+04
290	-0.09	0	-3.71E+05	54.75	0.34	3.97E+04
291	-0.01	0	-4.15E+05	30.66	0.2	2.35E+04
292	-0.13	0	-3.71E+05	47.9	0.27	4.28E+04
294	4.57E-03	1	-4.84E+05	6.15	0.1	1.50E+05
293	-0.12	0	-3.53E+05	42.58	0.27	3.97E+04
295	-1.09E-03	0	-4.55E+05	36.56	0.25	1.55E+05
296	-0.14	0	-4.66E+05	38.32	-0.06	1.79E+05
297	-0.06	4	-3.29E+05	68.66	0.47	8.73E+04
298	-0.06	4	-3.29E+05	68.66	0.47	8.73E+04
299	0.1	0	-3.62E+05	54.09	0.53	1.37E+05
300	-0.08	2	-3.94E+05	58.96	0.38	4.54E+04
301	0.09	2	-3.85E+05	34.84	0.17	8.12E+04
302	0.01	0	-3.23E+05	82.46	0.4	-1.30E+05
303	0.01	0	-3.20E+05	75.29	0.22	-1.09E+05
304	0.01	0	-3.06E+05	78.71	0.38	-2.03E+05
305	0.01	0	-3.13E+05	78.71	0.38	-1.64E+05
306	-0.01	0	-3.20E+05	61.85	0.31	-2.07E+05
307	0.02	0	-3.32E+05	72.15	0.35	-6.05E+04
308	-3.21E-04	0	-3.19E+05	78.71	0.38	-1.26E+05
309	-0.01	0	-3.20E+05	61.85	0.31	-2.07E+05
310	-0.01	0	-3.25E+05	61.85	0.31	-1.76E+05
311	-0.01	0	-3.20E+05	59.71	0.27	-2.08E+05
312	-0.01	0	-3.39E+05	61.85	0.31	-1.56E+05
313	0	0	-3.30E+05	59.71	0.19	-1.32E+05
314	-0.01	0	-3.30E+05	61.85	0.31	-1.46E+05
315	1.86E-03	0	-3.40E+05	57.72	0.29	-9.28E+04
316	-0.01	0	-3.39E+05	61.85	0.31	-1.56E+05
317	-0.01	0	-3.33E+05	64.14	0.32	-1.50E+05
318	0.01	0	-3.41E+05	61.85	0.31	-1.67E+05
319	-0.01	0	-3.79E+05	55.86	0.28	-1.62E+05
320	0.01	0	-3.77E+05	46.8	0.23	-1.03E+05
321	0.01	0	-3.60E+05	46.8	0.24	-1.63E+05
322	0.01	0	-3.65E+05	46.8	0.24	-1.30E+05
323	0.01	0	-3.74E+05	48.1	0.24	-1.05E+05
324	0.01	0	-3.61E+05	45.57	0.21	-1.58E+05
325	0.02	0	-3.77E+05	44.4	0.22	-3.76E+04
326	0.02	0	-3.70E+05	45.57	0.15	-8.33E+04
327	4.63E-03	0	-3.78E+05	46.8	0.23	-1.04E+05
234	0.01	0	-3.82E+05	46.8	0.23	-1.07E+05

235	0.03	0	-4.33E+05	51.34	0.36	1.10E+05
236	-2.01E-03	0	-4.31E+05	55.85	0.37	1.58E+05
237	-0.01	0	-4.09E+05	53.52	0.36	1.64E+04
238	-0.03	0	-4.39E+05	49.4	0.27	2.38E+05
239	0.03	0	-4.26E+05	47.23	0.21	1.36E+05
327	0.02	0	-4.26E+05	47.23	0.21	1.37E+05
329	-0.07	0	-4.30E+05	60.35	0.4	1.69E+05
330	-0.05	0	-5.06E+05	0	-0.18	1.31E+05
331	0.01	0	-4.82E+05	0	-0.13	1.55E+05
332	-0.03	0	-4.70E+05	0	-0.07	4.71E+04
333	0.03	0	-3.98E+05	0	-0.19	9.85E+04
334	-0.01	0	-3.91E+05	20.28	0.05	9.55E+04
335	-0.04	0	-3.77E+05	19.47	0.05	9.17E+04
336	0.02	0	-4.18E+05	0	-0.09	8.56E+04
337	0.04	0	-4.06E+05	0	-0.09	4.90E+04
338	0.04	0	-4.00E+05	0	-0.09	1.26E+04
339	-0.07	0	-4.25E+05	0	-0.18	-4.90E+05
340	0.01	0	-4.05E+05	0	-0.13	-4.36E+05
341	-0.04	0	-3.93E+05	0	-0.07	-5.12E+05
342	0.03	0	-3.35E+05	0	-0.19	-3.80E+05
343	-0.01	0	-3.30E+05	20.28	0.05	-3.67E+05
344	-0.04	0	-3.18E+05	19.47	0.05	-3.53E+05
345	0.03	0	-3.64E+05	0	-0.09	-3.25E+05
346	0.05	0	-3.54E+05	0	-0.09	-3.47E+05
347	0.05	0	-3.59E+05	0	-0.19	-2.83E+05
348	0.23	0	-5.61E+05	10.34	0.07	2.65E+05
349	0.06	0	-5.34E+05	9.04	-0.14	3.06E+05
350	0.06	0	-4.63E+05	37.09	-0.08	3.13E+05
351	0.01	0	-3.30E+05	0	0	-3.09E+05
269	0.05	0	-3.62E+05	53.81	0.15	1.09E+05
352	0.01	2	-2.93E+05	87.73	0.68	1.16E+05
353	-0.03	0	-2.81E+05	84.22	0.67	1.07E+05
354	0.03	2	-2.70E+05	77.98	0.51	1.06E+05
355	0.03	2	-2.84E+05	84.22	0.62	1.12E+05
356	0.05	0	-2.80E+05	68.8	0.37	8.85E+04
357	0.06	2	-3.25E+05	58.98	0.35	1.17E+05
358	0.02	0	-3.14E+05	56.94	0.34	1.10E+05

**Table S10.** Experimental and predicted values of anti-*L. amazonensis* activity. Residuals and influence values  $h$  ( $h^{\text{lim}} = 0.3125$ ) are reported. ^ validation group and \* test group

ID	Experimental activity	Predicted activity	Residuals	$h^{\text{lim}} = 0.3125$
222	0.62	1.22	-0.6	0.04
223	1.99	2.52	-0.53	0.03
224	1.6	0.99	0.61	0.02
225	1.67	1.25	0.42	0.02
69	1.9	1.85	0.05	0.02
226	0.95	1.13	-0.18	0.04
227	1.2	-0.62	1.82	0.03
228	1.26	-0.31	1.57	0.04
229	1.7	0.22	1.48	0.05
230	1.71	0.37	1.34	0.05
231	1.74	0.66	1.08	0.04
232	1.27	-0.89	2.16	0.03
233	1.55	0.42	1.13	0.02
234	0.02	0.38	-0.36	0.2
235	0.03	-0.14	0.17	0.2
236^	0.06	-0.3	0.36	0.21
237*	0.14	0.05	0.09	0.2
238	-0.3	-0.98	0.68	0.2
239*	-0.4	-1.35	0.95	0.2
240	0.24	0.51	-0.27	0.2
241*	1.3	1.3	0	0.06
242	0.9	-0.91	1.81	0.06
243	1.38	0.6	0.78	0.06
244^	1.36	0.49	0.87	0.12
245	1.48	0.26	1.22	0.04
246	1.45	0.48	0.97	0.04
247	0.7	-1.11	1.81	0.01
248	0.93	0.43	0.5	0.01
249^	0.85	-1.52	2.37	0.02
250	0.78	-1.16	1.94	0.01
251	1.34	-0.43	1.77	0.03
252	1.94	0.78	1.16	0.04
253	1.38	0.02	1.36	0.02
254	1.13	-1.42	2.55	0.03
255	1.67	0.27	1.4	0.03
256	1.52	-0.24	1.76	0.03



257	1.88	0.87	1.01	0.03
258	2.13	2.06	0.07	0.03
259	1.29	-0.45	1.74	0.03
260	1.09	-1.49	2.58	0.03
261	0.85	0.64	0.21	0.09
262	0.72	0.83	-0.11	0.19
263	-0.4	0.23	-0.63	0.22
264	-0.52	-1.91	1.39	0.32
265	1.84	-0.01	1.85	1
266*	0.89	-0.77	1.66	0.537
267^	-0.22	-1.21	0.99	0.31
268^	1.51	0.69	0.82	0.04
269*	1.8	1.71	0.09	0.04
270	1.5	-0.46	1.96	0.03
271	1.78	1.52	0.26	0.04
272*	1.45	-1.13	2.58	0.06
273	1.38	0.91	0.47	0.06
274	1.46	-0.65	2.11	0.05
275	1.63	-0.47	2.1	0.05
276	1.62	0.65	0.97	0.04
277	1.34	-0.9	2.24	0.05
278^	1.29	-0.99	2.28	0.04
279	1.72	0.12	1.6	0.04
280	1.45	-0.48	1.93	0.03

**Table S11.** *Experimental* and predicted values of anti-L. infantum activity. Residuals and influence values  $h$  ( $h^{\text{lim}} = 0.24$ ) are reported. ^ validation group and \* test group

ID	Experimental activity	Predicted activity	Residuals	$h^{\text{lim}} = 0.24$
281^	1.13	0.13	1	0.13
282	1.26	0.03	1.23	0.06
283*	1.38	1.52	-0.14	0.06
284	1.29	0.48	0.81	0.15
285	2.1	1.12	0.98	0.07
286	1.21	0.2	1.01	0.07
222	0.35	0.12	0.23	0.03
223	1.45	-0.33	1.78	0.1
287^	1.65	1.5	0.15	0.03
288	1.82	0.45	1.37	0.07
224	1.41	0.18	1.23	0.06
225	1.59	1.44	0.15	0.02
289	1.74	0.04	1.7	0.09
69	2.13	0.96	1.17	0.07
290	0.08	0.04	0.04	0.07
291	0.46	0.19	0.27	0.04
292	-0.15	0.33	-0.48	0.12
294^	0	0.04	-0.04	0.12
293	-0.15	0.66	-0.81	0.11
295	0.65	1.07	-0.42	0.06
296	-0.1	-1.07	0.97	0.24
297	0.72	-0.89	1.61	0.34
298	1.13	0.34	0.79	0.04
299	0.38	0.46	-0.08	0.18
300	0.43	-0.68	1.11	0.11
301	2.09	1.06	1.03	0.15
302	1.88	-0.29	2.17	0.05
303	1.93	-0.83	2.76	0.09
304*	2.11	-0.05	2.16	0.06
305	2.28	0.61	1.67	0.05
306	0.93	-1.7	2.63	0.04
307	2.28	1.47	0.81	0.03
308	1.32	-1.16	2.48	0.04
309	1.46	-0.51	1.97	0.04
310	1.65	0.14	1.51	0.03
311*	1.86	0.24	1.62	0.04

312	1.84	0.66	1.18	0.03
313	1.77	-0.2	1.97	0.04
314*	0.96	-1.15	2.11	0.03
315	1.42	0.23	1.19	0.02
316	1.44	-0.24	1.68	0.03
317*	1.49	-0.17	1.66	0.03
318^	1.44	-0.64	2.08	0.03
319	2.03	0.99	1.04	0.03
320^	1.69	0.82	0.87	0.02
321	1.71	0.46	1.25	0.03
322*	1.6	0.44	1.16	0.02
323	1.31	-0.09	1.4	0.02
324*	2.08	1.18	0.9	0.02
325	0.91	-0.4	1.31	0.02
326	1.75	0.38	1.37	0.02
327	1.92	1.33	0.59	0.02
234	0.08	-2.93	3.01	0.02
235	0	-1.43	1.43	0.06
236	0.26	-0.22	0.48	0.06
237	0.3	-0.9	1.2	0.04
238	0.34	0.74	-0.4	0.07
239	0.15	-1.72	1.87	0.03
327*	0.68	-0.41	1.09	0.03
329	-0.3	-0.41	0.11	0.09
330	0.73	0.97	-0.24	0.13
331	0.56	0.45	0.11	0.09
332^	0.38	0.39	-0.01	0.08
333	0.49	-0.14	0.63	0.07
334	0.34	0.35	-0.01	0.03
335	-0.4	-0.8	0.4	0.04
336	0.11	-0.39	0.5	0.06
337*	0.28	-0.5	0.78	0.05
338	0.04	-1.23	1.27	0.05
339^	2.26	0.26	2	0.17
340	1.7	-1.26	2.96	0.12
341	2.18	0.58	1.6	0.15
342*	1.71	-0.91	2.62	0.11
343	1.45	-0.48	1.93	0.07
344	2.14	1.79	0.35	0.07
345	2.29	1.5	0.79	0.08
346	2.19	0.86	1.33	0.09

347	2.1	0.28	1.82	0.09
348	1.28	-0.31	1.59	0.35
349	0.57	-0.36	0.93	0.13
350	2.07	1.84	0.23	0.15
351	0.62	-0.76	1.38	0.08
269	0.92	-0.98	1.9	0.05
352^	-0.15	-1.93	1.78	0.13
353	-0.52	-0.63	0.11	0.12
354	0.9	-0.46	1.36	0.11
355	1.75	1.78	-0.03	0.12
356	-0.1	-2.15	2.05	0.04
357^	0.92	-0.89	1.81	0.11
358	0.91	1.2	-0.29	0.03

**Table S12.** Values predicted by the QSAR models of antileishmanial activity of the 68 naphthoquinone derivatives (prediction group).

ID	Predicted <i>anti-L. amazonensis</i> activity	<i>h</i> *	Predicted anti- <i>L. infantum</i> activity	<i>h</i> *
1	1.18	0.02	1.13	0.07
2	1.34	0.03	2.29	0.2
3	1.35	0.03	1.08	0.02
4	1.27	0.03	1.33	0.03
5	1.32	0.03	1.27	0.21
6	1.34	0.03	0.1	0.08
7	1.28	0.03	0.35	0.08
8	1.27	0.02	1.98	0.2
9	1.29	0.03	0.8	0.05
10	1.23	0.03	1.11	0.06
11	1.27	0.02	2.1	0.18
12	1.29	0.03	1.11	0.06
13	1.23	0.03	1.36	0.07
14	1.3	0.02	0.58	0.08
15	1.34	0.03	0.29	0.05
16	1.23	0.03	0.63	0.06
17	1.39	0.03	-0.05	0.09
18	1.29	0.02	1.32	0.09
19	1.33	0.03	1.03	0.06
20	1.22	0.03	1.06	0.06
21	1.24	0.03	1.09	0.1

22	1.29	0.03	0.85	0.07
23	1.23	0.03	0.89	0.08
24	1.22	0.03	0.87	0.1
25	1.25	0.03	0.67	0.07
26	1.17	0.03	0.73	0.08
27	1.16	0.02	2.33	0.31
28	1.32	0.03	3.13	0.57
29	1.33	0.03	2.41	0.33
30	1.25	0.03	2.34	0.33
31	1.29	0.03	2.1	0.37
32	1.32	0.03	1.42	0.15
33	1.26	0.03	1.34	0.17
34	1.25	0.02	2.96	0.42
35	1.26	0.03	2.26	0.2
36	1.2	0.03	2.23	0.23
37	1.25	0.02	3.18	0.39
38	1.26	0.03	2.63	0.22
39	1.2	0.03	2.54	0.24
40	1.28	0.02	1.85	0.33
41	1.31	0.03	1.35	0.22
42	2.67	0.94	1.68	0.27
43	2.9	1.09	1.09	0.33
44	1.22	0.02	2.64	0.34
45	1.19	0.03	1.88	0.27
46	1.19	0.03	1.6	0.28
47	1.18	0.03	0.87	0.3
48	1.27	0.02	2.44	0.24
49	1.3	0.03	2.21	0.25
50	1.2	0.03	2.25	0.25
51	1.22	0.03	2.16	0.21
52	1.27	0.03	1.98	0.22
53	1.22	0.02	2.64	0.12
54	1.19	0.03	1.88	0.07
55	1.19	0.03	1.6	0.17
56	1.18	0.03	0.87	0.14
57	1.16	0.02	2.2	0.16
58	1.16	0.03	1.93	0.13
59	1.13	0.03	1.94	0.17
60	1.13	0.03	1.73	0.14
61	1.14	0.03	1.73	0.16
62	1.11	0.03	1.56	0.15

63	1.32	0.03	1.05	0.07
64	2.57	0.68	1.08	0.06
65	1.37	0.03	0.79	0.04
66	1.35	0.03	1.73	0.12
67	2.65	0.73	1.14	0.05
68	2.68	0.75	1.31	0.05

**Table S13.** Intercorrelation matrix of the QSAR model descriptors for toxicity.

Descriptor	$d_1$	$d_2$	$d_3$	$d_4$	$d_5$	VIF
$d_2$	1	4.05E-03	0.03	0.07	5.03E-04	1.04
$d_2$		1	0.18	2.05E-05	0.10	1.08
$d_3$			1	0.22	0.44	1.53
$d_4$				1	0.31	1.28
$d_5$				0.31	1	1.39

**Table S14.** Numerical values of the QSAR toxicity model descriptors.

ID	$d_1$	$d_2$	$d_3$	$d_4$	$d_5$
1	4.44	0.22	1.67	15.60	0.73
2	4.67	0.65	1.70	9.26	0.62
3	4.79	0.87	1.67	9.43	0.76
4	4.80	0.94	1.66	9.50	0.80
5	5.01	0.76	1.69	16.83	0.81
6	5.13	0.91	1.66	17.23	0.94
7	5.15	0.98	1.66	17.31	0.99
8	4.83	1.03	1.62	11.13	0.83
9	4.87	0.75	1.61	11.73	0.88
10	4.87	0.78	1.61	11.83	0.89
11	4.68	-0.02	1.68	6.70	0.89
12	4.87	-0.21	1.65	7.03	0.91
13	4.87	-0.15	1.64	7.08	0.91
14	5.14	1.26	1.81	8.70	1.26
15	5.18	0.76	1.76	8.57	1.29
16	5.19	0.71	1.73	8.55	1.29
17	5.94	0.41	1.86	3.85	1.82
18	4.79	0.27	1.64	16.33	0.92
19	4.89	0.11	1.62	16.27	0.91
20	4.87	0.08	1.62	16.32	0.91
21	5.22	0.46	1.63	17.06	1.11
22	5.32	0.28	1.61	17.00	1.10
23	5.30	0.24	1.60	17.05	1.10

24	5.64	0.62	1.61	17.65	1.30
25	5.73	0.43	1.59	17.73	1.28
26	5.72	0.37	1.58	17.77	1.28
27	1.88	0.37	1.68	11.18	0.94
28	2.18	0.77	1.70	7.18	0.79
29	2.27	1.00	1.67	7.28	0.94
30	2.28	1.08	1.67	7.18	0.99
31	2.50	0.89	1.70	10.52	0.98
32	2.59	1.05	1.67	11.15	1.13
33	2.60	1.13	1.66	11.29	1.18
34	2.25	1.14	1.62	6.58	1.03
35	2.28	0.88	1.62	7.05	1.10
36	2.28	0.92	1.62	7.09	1.11
37	2.15	0.08	1.68	8.76	1.10
38	2.28	-0.11	1.65	8.57	1.13
39	2.28	-0.05	1.64	8.55	1.13
40	2.57	1.40	1.81	9.30	1.50
41	0.44	0.83	1.99	11.83	1.56
42	0.45	0.78	1.94	11.90	1.55
43	3.31	0.50	1.86	3.86	2.07
44	1.95	-0.87	3.45	17.08	-0.13
45	1.94	-0.77	3.41	16.89	0.01
46	2.29	-0.74	3.44	2.21	0.03
47	2.28	-0.66	3.40	2.11	0.17
48	2.22	0.42	1.64	11.62	1.14
49	2.29	0.24	1.63	11.86	1.13
50	2.28	0.21	1.63	11.95	1.13
51	2.61	0.61	1.63	12.47	1.33
52	2.68	0.42	1.61	12.63	1.32
53	2.67	0.37	1.61	12.72	1.32
54	2.98	0.78	1.61	12.99	1.53
55	3.05	0.57	1.59	13.38	1.51
56	3.04	0.51	1.58	13.46	1.51
57	1.81	-0.50	3.45	2.29	0.39
58	1.79	-0.56	3.43	2.68	0.39
59	2.19	-0.37	3.44	2.87	0.55
60	2.17	-0.43	3.41	2.81	0.55
61	2.56	-0.25	3.42	2.97	0.72
62	2.54	-0.32	3.37	2.92	0.72
63	3.34	-0.09	1.63	6.37	1.53
64	3.66	0.12	1.58	5.31	1.69
65	3.66	0.10	1.58	5.24	1.69

66	3.64	0.35	1.58	4.99	1.68
67	3.97	0.09	1.53	3.68	1.84
68	3.95	-0.36	1.53	4.00	1.84
359	4.95	1.50	1.56	6.16	1.61
360	4.94	1.64	1.56	3.95	0.94
361	5.32	1.69	1.53	9.09	1.79
362	4.83	0.61	1.54	6.31	1.29
363	5.75	0.39	1.73	13.73	0.23
364	4.88	0.64	1.52	6.38	1.31
365	1.22	-0.05	1.41	5.57	-0.01
366	1.38	-0.08	1.39	7.96	-0.07
367	7.54	1.75	1.50	12.95	1.84
368	7.37	0.69	1.40	18.81	1.52
369	7.37	1.31	1.42	16.03	1.52
370	7.37	0.77	1.38	18.04	1.52
371	7.13	1.22	1.41	20.24	1.51
372	7.35	1.53	1.36	9.49	1.51
373	7.53	1.80	1.52	12.97	1.85
374	7.35	0.63	1.41	19.02	1.52
375	6.26	0.75	1.96	6.45	1.15
376	2.37	1.18	0.98	5.31	0.42
377	4.00	0.95	1.34	1.81	1.38
160	3.09	0.23	1.33	3.38	0.93
78	4.79	1.71	1.36	5.87	2.70
162	4.78	1.37	1.32	5.88	1.87
378	4.94	0.06	2.93	0.93	-0.66
379	5.37	0.31	2.92	0.12	-0.55
380	5.75	0.36	2.91	1.37	-0.45
381	5.85	0.62	2.89	1.42	-0.45
382	6.37	0.98	2.84	1.49	-0.34
383	6.14	1.22	2.77	5.50	0.62
384	6.22	0.62	2.88	0.17	-0.35
385	6.12	0.41	2.88	2.65	-0.35
386	6.59	0.65	2.86	1.81	-0.25
387	5.36	0.32	2.47	1.59	-0.02
388	5.84	0.47	2.82	0.68	-0.45
389	6.22	0.61	2.81	0.79	-0.35
390	7.20	0.84	2.78	2.29	-0.06
391	7.80	0.89	2.24	1.96	-0.04
392	7.35	0.61	2.65	1.40	-0.21
393	8.77	1.10	2.26	2.24	0.19
394	7.69	0.67	2.59	1.59	-0.11



395	8.44	0.90	2.52	2.05	0.07
396	7.69	0.18	2.57	5.01	-0.08
397	7.91	-0.21	2.54	6.85	-0.02
398	7.72	0.01	2.57	1.93	-0.11
399	8.08	-0.22	2.52	7.79	-0.01
400	8.79	-0.02	2.46	6.80	0.05
401	9.15	-0.35	2.41	5.45	0.26
402	4.46	0.22	3.78	2.90	-0.35
403	5.03	-0.34	2.88	0.87	-0.50
404	3.86	0.16	3.38	1.50	-0.35
405	4.24	-0.27	2.94	1.14	-0.41
406	4.69	-0.31	2.82	0.85	-0.27
407	4.85	-0.26	2.82	1.00	-0.22
408	2.65	-0.90	3.00	0.46	-0.48
409	4.04	1.50	1.99	3.33	0.08
410	3.57	1.43	2.01	3.78	0.00
411	3.63	1.27	2.05	-0.16	-0.09
412	4.43	1.71	2.02	0.62	0.23
413	4.17	1.56	2.15	3.00	0.18
414	3.70	1.48	2.21	1.47	0.01
415	3.75	1.34	2.21	0.67	0.02
416	4.57	1.77	2.17	2.01	0.33
191	3.38	1.61	1.90	-1.25	1.17
417	2.97	1.40	1.94	1.96	1.00
418	3.76	1.84	1.91	3.80	1.43
419	5.53	1.82	1.61	3.77	0.22
420	6.45	1.45	1.53	0.72	0.61
421	6.20	1.46	1.55	9.30	0.13
422	5.49	-0.11	2.62	9.82	1.54
423	6.73	1.11	2.25	6.97	2.11
424	5.11	-0.57	2.43	10.13	2.62
425	5.63	1.81	1.14	3.95	2.17
426	5.63	0.40	1.16	11.86	2.18
427	5.63	0.03	1.18	12.77	2.19
428	5.68	1.73	1.33	11.50	2.58
429	5.25	0.51	1.17	1.40	1.99
430	6.12	0.34	1.41	1.09	0.91

**Table S15.** Experimental and predicted values of toxicity. Residuals and influence values  $h$  ( $h^{\text{lim}} = 0.3125$ ) are reported. ^ validation group and \* test group

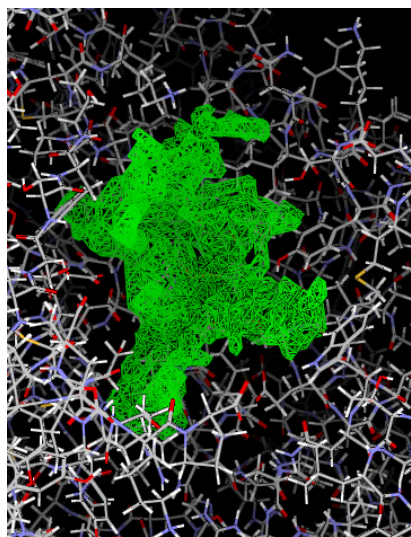
ID	Experimental activity	Predicted activity	Residuals	$h^{\text{lim}} = 0.3125$
359	0.70	0.61	0.09	0.05
360	0.59	-1.15	1.73	0.04
361*	1.10	3.96	-2.86	0.06
362	0.92	0.65	0.27	0.03
363	0.92	0.11	0.81	0.42
364^	0.82	0.16	0.66	0.03
365	0.72	-0.29	1.00	0.06
366	0.83	0.88	-0.05	0.1
367^	0.14	-1.72	1.86	0.08
368	0.38	0.01	0.37	0.14
369	0.36	0.11	0.26	-0.15
370^	0.27	-0.72	0.99	0.13
371	-0.13	-1.80	1.67	0.19
372^	0.51	-0.71	1.22	0.07
373	0.66	1.35	-0.69	0.08
374	0.58	1.17	-0.59	0.15
375	1.14	0.22	0.92	0.02
376	0.52	0.57	-0.06	0.04
377^	0.98	1.18	-0.20	0.05
160	0.79	-0.21	1.00	0.02
78	0.38	0.57	-0.19	0.13
162	0.45	-0.17	0.62	0.06
378	2.07	0.23	1.84	0.06
379*	2.03	-0.11	2.13	0.05
380	1.90	-0.51	2.41	0.05
381	1.90	-0.22	2.12	0.05
382	1.93	0.31	1.62	0.05
383	1.21	-1.23	2.44	0.04
384^	2.00	-0.09	2.09	0.05
385	2.20	1.51	0.68	0.04
386*	1.90	-0.29	2.19	0.04
387	1.98	1.56	0.43	0.03
388	1.60	-2.17	3.77	0.04
389	1.93	-0.21	2.13	0.04
390	1.90	0.07	1.83	0.04
391	2.08	1.86	0.22	0.07
392*	1.61	-2.11	3.72	0.05
393	1.61	0.10	1.51	-0.94

394	1.90	-0.27	2.17	0.06
395	1.86	-0.27	2.13	0.08
396	2.00	0.73	1.27	0.05
397	1.83	-0.25	2.07	0.08
398	2.12	0.30	1.82	0.08
399	1.65	-1.12	2.77	0.08
400	1.86	-0.17	2.03	0.09
401	2.05	0.24	1.81	0.14
402	2.25	0.79	1.46	0.15
403*	2.24	0.93	1.32	0.07
404	2.09	0.63	1.46	0.12
405*	2.07	0.56	1.51	0.08
406^	1.65	-1.90	3.55	0.07
407	2.06	0.55	1.51	0.06
408	1.70	-1.76	3.46	0.16
409	1.11	0.35	0.76	0.06
410	0.67	-2.00	2.67	0.07
411	1.61	1.96	-0.34	0.05
412	1.12	0.07	1.05	-0.28
413*	0.89	-1.26	2.15	0.07
414*	0.84	-2.10	2.94	0.07
415	1.28	0.01	1.26	0.06
416	1.33	1.07	0.26	0.07
191	0.74	0.10	0.63	-1.24
417^	0.48	-2.14	2.62	0.08
418	0.74	0.44	0.30	0.09
419	0.82	-0.82	1.64	0.08
420	1.43	1.42	0.01	0.08
421	0.69	-0.45	1.14	0.11
422	1.13	-0.45	1.58	0.11
423	1.11	0.72	0.40	0.08
424	0.93	-0.37	1.30	0.27
425	0.19	-1.55	1.74	0.11
426	0.52	0.79	-0.28	0.08
427	0.41	-0.04	0.45	0.10
428	0.06	-0.34	0.40	0.1
429	0.93	0.47	0.46	0.14
430	0.98	-1.63	2.61	0.08

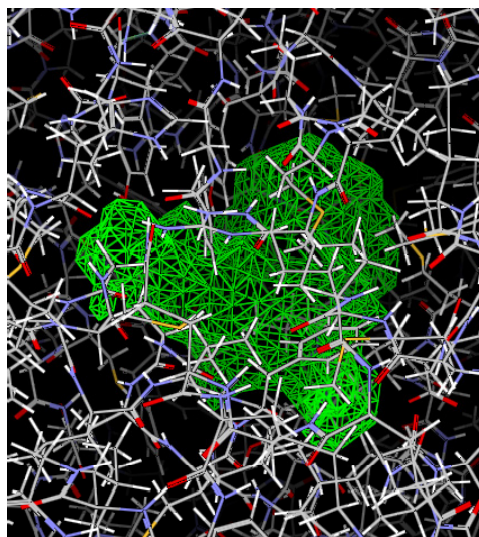
**Table S16.** Values predicted by the QSAR model of toxicity of the 68 naphthoquinone derivatives (prediction group).

ID	Predicted activity	$h^{\text{lim}=0.3}$
1	0.55	0.14
2	0.81	0.04
3	0.74	0.04
4	0.71	0.04
5	0.43	0.16
6	0.36	0.17
7	0.33	0.17
8	0.60	0.06
9	0.62	0.06
10	0.61	0.06
11	1.02	0.03
12	1.05	0.04
13	1.03	0.04
14	0.70	0.04
15	0.78	0.03
16	0.79	0.03
17	1.11	0.10
18	0.49	0.14
19	0.54	0.14
20	0.54	0.14
21	0.43	0.14
22	0.48	0.14
23	0.48	0.14
24	0.37	0.14
25	0.41	0.14
26	0.42	0.14
27	0.42	0.14
28	0.59	0.08
29	0.51	0.08
30	0.49	0.09
31	0.41	0.12
32	0.32	0.13
33	0.28	0.13
34	0.48	0.08
35	0.50	0.08
36	0.49	0.08
37	0.59	0.10
38	0.64	0.10
39	0.63	0.09

40	0.32	0.14
41	0.14	0.32
42	0.13	0.31
43	0.76	0.13
44	1.23	0.61
45	1.18	0.59
46	1.92	0.25
47	1.87	0.25
48	0.38	0.13
49	0.40	0.13
50	0.41	0.14
51	0.30	0.13
52	0.33	0.13
53	0.34	0.13
54	0.24	0.13
55	0.26	0.13
56	0.27	0.13
57	1.75	0.29
58	1.74	0.29
59	1.71	0.27
60	1.71	0.27
61	1.68	0.25
62	1.68	0.25
63	0.78	0.08
64	0.77	0.08
65	0.78	0.08
66	0.74	0.07
67	0.85	0.10
68	0.92	0.14



(a)



(b)

**Figure S1.** Cavities in the active site of *TcTR* (a) and *TcLαD* (b) proteins.

**Table S17.** Results of the coupling of naphthoquinone derivatives in the active site of the *TcTR* and *TcLaD* proteins.

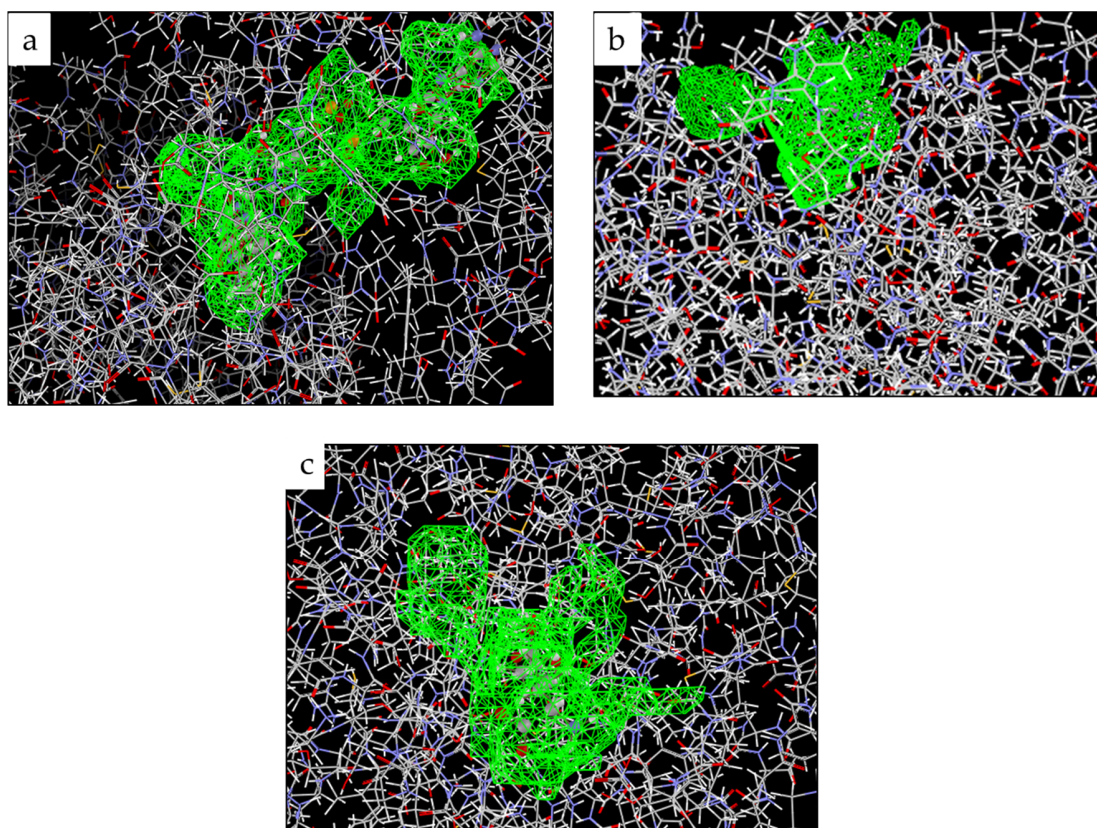
Ligand	<i>TcTR</i>				<i>TcLaD</i>			
	Energy (kcal/mol)	Hydrogen bonds (HB)			Energy (kcal/mol)	Hydrogen bonds (HB)		
		Residues	Distance (Å)	Force		Residues	Distance (Å)	Force
1	-93.2095	Lys 62 A	3.27	-1.60	-79.966	-		
		Ser 464 B	2.78	-2.50				
2	-93.1213	-			-101.396	Tyr 103 B	3.12	-2.4
3	-97.3813	Lys 62 A	3.25	-1.75	-102.118	-		
		Ser 464 B	2.69	-2.50				
4	-98.8420	Lys 62 A	2.93	-2.50	-89.6888	-		
		Ser 464 B	2.84	-2.50				
		Thr 463 B	3.35	-1.15				
5	-96.1777	Asn 340 A	3.12	-2.39	-99.6799	Tyr 103 B	3.34	-1.31
6	-108.0890	Lys 62 A	2.94	-2.50	-113.434	-		
		Ser 464 B	2.84	-2.50				
		Thr 463 B	3.32	-1.31				
7	-101.9060	Lys 62 A	3.27	-1.67	-93.4699	-		
		Ser 464 B	2.86	-2.50				
8	-91.5210	Lys 62 A	2.95	-2.05	-80.5908	-		
		Ser 464 B	2.60	-2.39				
		Thr 463 B	3.30	-1.48				
9	-96.9612	Lys 62 A	2.94	-2.50	-89.3261	-		
		Ser 464 B	2.84	-2.50				
		Thr 463 B	3.28	-1.54				
10	-94.0496	Lys 62 A	3.28	-1.58	-86.8946	-		
		Ser 464 B	2.78	-2.50				
11	-90.5348	Ser 464 B	2.68	-2.50	-94.7798	-		
12	-96.7141	Lys 62 A	2.94	-2.50	-97.2161	-		
		Ser 464 B	2.84	-2.50				
		Thr 463 B	3.30	-1.43				
13	-95.6654	Lys 62 A	3.19	-1.83	-92.1773	Tyr 116 B	2.77	-2.50
		Ser 464 B	2.82	-2.50		Tyr 103 B	2.76	-2.50
		Thr 463 B	3.37	-1.05				
14	-103.9370	Ser 464 B	2.48	-1.54	-108.916	Tyr 116 B	3.03	-2.5
15	-100.7810	Lys 62 A	3.20	-1.90	-109.628	Tyr 116 B	3.18	-2.08
		Ser 464 B	2.83	-2.50				
		Thr 463 B	3.29	-1.51				
16	-90.6406	Lys 62 A	2.78	-0.94	-90.6885	Tyr 103 B	3.47	-0.65
			3.12	-1.48				

17	-111.5950	Ser 464 B	2.99	-0.70	-96.9022	-		
		Leu 399 B	2.48	-1.48				
18	-88.1999	Ser 464 B	3.0700	-2.4200	-84.9483	-		
19	-93.0333	Lys 62 A	3.24	-1.80	-102.487	-		
		Ser 464 B	2.80	-2.50				
20	-87.2394	-			-88.8781	-		
21	-102.4510	Lys 62 A	3.37	-1.04	-90.7122	-		
		Ser 464 B	2.72	-2.50				
22	-101.7750	Lys 62 A	3.13	-2.37	-94.9361	Tyr 116 B	3.22	-1.89
		Ser 464 B	2.78	-2.50				
23	-99.1009	Lys 62 A	3.16	-2.13	-95.958	Tyr 116 B	2.71	-2.50
		Ser 464 B	2.84	-2.50		Tyr 103 B	2.72	-2.50
						HEM_1450 B	0	-0.21
24	-102.5440	Ser 464 B	2.65	-2.50	-107.877	-		
25	-97.5418	Glu 467 B	3.22	-1.88	-108.501	-		
26	-100.7280	Lys 62 A	2.93	-2.50	-98.0511	Tyr 116 B	2.65	-2.5
		Ser 464 B	2.84	-2.50				
		Thr 463 B	3.35	-1.11				
27	-87.9757	Lys 62 A	3.27	-1.64	-82.1982	-		
		Ser 464 B	3.77	-2.5				
		Thr 463 B	2.90	-2.5				
28	-95.2882	Lys 62 A	2.94	-2.12	-91.0531	Tyr 103 B	3.08	-1.82
		Ser 464 B	2.58	-2.32				
		Thr 463 B	3.22	-1.83				
29	-100.6680	Lys 62 A	2.98	-2.5	-95.5983	-		
		Ser 464 B	2.83	-2.5				
		Thr 463 B	3.25	-1.27				
30	-98.5385	Lys 62 A	3.12	-1.27	-90.1862	HEM_1450 B	0	-2.5
		Ser 464 B	2.57	-2.22				
		Thr 463 B	3.19	-1.79				
31	-91.1649	Ser 464 B	3.28	-1.61	-97.5895	-		
32	-99.3677	Gly 459 B	3.11	-2.33	-107.973	-		
		Arg 355 A	2.63	-2.50				
33	-101.1350	Lys 62 A	3.18	-1.04	-100.14	Met 360 B	3.04	-1.25
		Ser 464 B	2.77	-2.50		HEM_1450 B	0	-2.5
		Thr 463 B	3.30	-1.02				
34	-90.2534	Lys 62 A	3.43	-0.76	-85.9238	-		
		Ser 464 B	2.78	-2.50				
35	-95.1599	Lys 62 A	3.03	-2.25	-96.4178	-		
		Ser 464 B	2.79	-2.50				



		Thr 463 B	3.22	-1.42				
36	-92.4304	Lys 62 A	3.27	-1.67	-87.0079	HEM_1450 B	0	-2.48
		Ser 464 B	2.62	-2.50				
37	-89.9000	Lys 62 A	3.39	-0.93	-90.2266	-		
		Ser 464 B	2.85	-2.50				
38	-91.8954	Glu 466 B	2.84	-1.16	-95.5077	Met 360 B	3.18	-0.99
			3.34	-1.30		HEM_1450 B	0	-2.15
			2.64	-2.22		Met 358 B	3.16	-2.18
39	-92.2933	Ser 464 B	2.59	-2.38	-86.5687	Tyr 103 B	2.56	-2.17
		Thr 463 B	3.20	-1.66				
40	-98.1876	Arg 472 B	2.67	-2.50	-79.3277	Tyr 103 B	2.97	-2.5
			3.29	-1.55				
			3.07	-1.82				
		Tyr 455 B	2.99	-1.53				
		Thr 457 B	2.71	-0.75				
41	-98.3294	Lys 62 A	2.97	-2.50	-105.707	Tyr 116 B	3.13	-2.37
		Ser 464 B	2.84	-2.50				
		Thr 463 B	3.26	-1.24				
42	-99.5445	Gly 459 B	3.10	-1.17	-92.1493	Tyr 116 B	2.92	-2.50
		His 461 B	2.57	-1.18		Met 358 B	3.39	-1.03
						Tyr 103 B	3.11	-1.09
							2.79	-2.50
43	-110.8730	Leu 399 B	2.96	-0.81	-99.1137	-		
		Ser 464 B	2.49	-1.57				
		Thr 463 B	3.06	-2.50				
44	-87.7661	Gly 459 B	2.66	-2.15	-99.1828	Tyr 116 B	2.93	-2.50
		Arg 472 B	3.13	-1.42			2.78	-1.74
		Glu 466 B	3.33	-0.72		Tyr 103 B	2.79	-2.50
45	-101.9210	Ser 464 B	2.56	-2.20	-96.7045	-		
		Thr 463 B	3.96	-0.70				
46	-100.4100	Ser 464 B	2.55	-2.07	-106.116	-		
		Lys 62 A	3.20	-1.93				
47	-102.4440	His 461 B	2.60	-1.56	-100.698	Tyr 103 B	2.65	-2.5
48	-84.4483	Asn 340 A	2.85	-2.50	-92.4174	Tyr 116 B	3.11	-2.47
		Thr 457 B	2.72	-2.50		Tyr 103 B	2.70	-2.50
		Ser 470 B	3.21	-0.98			2.48	-1.81
49	-91.8201	Ser 464 B	2.78	-2.50	-94.2563	-		
50	-93.6531	Thr 463 B	3.26	-1.71	-84.7217	Tyr 103 B	3.12	-2.42
51	-93.4097	Ser 464 B	2.50	-1.70	-96.9773	Tyr 103 B	3.05	-0.92

52	-99.7175	Ser 464 B	2.68	-2.50	-96.1798	-		
		Lys 62 A	3.19	-1.35				
53	-89.8147	Lys 62A	3.02	-2.07	-86.3019	Tyr 103 B	2.83	-2.5
		Ser 464 B	2.56	-2.2				
54	-91.1998	Lys 62A	3	-2.31	-84.2155	Tyr 103 B	2.98	-2.5
		Ser 464 B	2.63	-2.5				
55	-90.4967	Asn 340	2.97 3.02	2.5 -2.5	-89.4427	Tyr 103 B	3.03	-2.5
56	-92.4062	Asn 340 A	2.98	-2.5	-95.4859	Tyr 103 B	2.69	-2.34
		Gly 459 B	2.82	2				
57	-79.6845	Ser 464 B	3.11	-2.40	-80.471	Tyr 103 B	2.85	-4.02
							2.99	
58	-81.9298	Arg 355 A	2.45	-0.97	-82.6084	Tyr 103 B	2.75	-2.46
			2.86	-0.90			3.13	-2.13
		Asn 340 A	3.18	-2.08				
59	-90.5529	Lys 62 A	3.05	-2.03	-88.3182	Tyr 103 B	2.84	-2.5
		Ser 464 B	2.55	-2.12			3.08	-2.5
60	-91.8292	Lys 62 A	2.96	-2.21	-90.6668	Tyr 103 B	2.75	-2.5
		Ser 464 B	2.65	-2.50			3.16	-1.77
61	-91.2961	Asn 340A	3.14 2.84	-0.81 -2.50	-90.6484	Tyr 103 B	2.9	-2.5
62	-94.5097	Asn 340A	2.98 3.16	-0.83 -2.21	-92.0233	Tyr 103 B	3.04	-2.4
63	-120.0300	Ser 15 A	3.01	2.20	-112.45	HEM_1450 B	0	-2.06
						Tyr 103 B	3.05	-0.71
							3.08	-2.5
							2.58	-1.39
64	-128.7530	Asn 340 A	2.59	-2.41	-116.652	HEM_1450 B	0	-2.21
		Gly 459 B	2.64	-2.50		Tyr 103 B	2.77	-1.46
		Arg 355 A	3.02	-2.06			3.12	-2.41
65	-122.4240	Ser 15 A	3.08	-2.50	-114.785	HEM_1450 B	0	-2.5
66	-124.3250	Ser 15 A	3.02	-2.08	-121.598	Tyr 103 B	3.09	-1.79
							3.10	-2.50
							3.06	-2.50
67	-123.3630	Ser 15 A	3.10	-2.50	-107.714	-		
68	-123.5650	Ser 15 A	3.11	-2.45	-121.185	HEM_1450 B	0	-2.5



**Figure S2.** Cavities in the active site of LTR (a), *LaA* (b), and *LiTA* (c) proteins.



							Asp 327	3.53	-0.02
8	-100.768	Lys 60	3.10	-1.85	42	-114.535	Ser 14	3.04	-1.51
							Gly 15	2.92	-2.50
							Thr 335	3.35	-0.22
								3.07	-1.82
								3.08	-2.50
							Asp 327	2.85	-2.08
9	-107.033	Lys 60	2.65	-0.84	43	-101.908	Thr 335	3.00	-2.50
								3.06	-0.63
							Ser 162	2.54	-0.94
								3.50	-0.15
							Arg 287	3.30	-0.62
								3.40	-0.42
								2.71	-1.96
								3.15	-0.05
							Ser 14	3.03	-2.11
								2.80	-2.50
							Lys 60	2.78	-1.75
10	-114.045	Lys 60	3.08	-1.99	44	-112.801	Arg 287	3.02	-2.50
11	-106.527	Lys 60	2.51	-0.61	45	-93.208	Thr 335	2.85	-2.50
							Arg 287	3.10	-2.48
							Asp 327	2.98	-2.50
							Ser 162	2.97	-2.50
								2.89	-2.50
								2.75	-2.50
12	-112.686	Lys 60	3.06	-1.86	46	-109.701	Ser 14	2.73	-2.50
							Ser 162	3.10	-2.13
								3.58	-0.09
							Arg 287	3.05	-2.15
							Thr 335	2.95	-2.50
								2.77	-2.50
13	-108.036	Lys 60	2.62	-0.87	47	-114.397	Ser 14	2.72	-2.50
							Ser 162	3.16	-2.21
								3.22	-1.89
							Arg 287	3.11	-2.31
							Thr 335	3.32	-1.38
								3.08	-2.29
14	-111.703	Lys 60	3.07	-0.69	48	-93.423	Lys 60	2.85	-1.49
			2.64	-0.98					
15	-121.911	Ser 14	3.28	-1.45	49	-106.004	Lys 60	3.43	-0.62

			3.06	-2.50					
		Thr 51	3.03	-0.59					
		Cys 52	2.84	-2.50					
		Lys 60	3.37	-1.04					
16	-116.118	Lys 60	2.75	-1.72	50	-107.717	Arg 287	2.97	-2.50
		Thr 51	2.86	-2.50					
		Thr 335	2.85	-1.46					
			3.04	2.50					
17	-127.261	Ser 14	3.21	-1.93	51	-109.342	Lys 60	3.60	-0.01
		Thr 335	2.92	-2.50			Arg 287	3.14	-2.31
			2.96	-1.77					
			3.59	-0.07					
		Lys 60	2.62	-0.99					
		Ser 162	3.02	-2.31					
			3.42	-0.92					
		Arg 287	2.90	-2.25					
18	-96.817	Lys 60	2.61	-2.50	52	-109.544	Arg 287	2.91	-2.50
19	-113.030	Lys 60	3.06	-2.50	54	-114.265	Thr 51	2.74	-2.40
								3.18	-1.22
							Thr 335	2.93	-2.50
								3.08	-1.56
20	-114.556	Lys 60	3.03	-2.50	54	-118.580	Cys 52	3.07	-0.90
							Thr 51	2.60	-1.74
								3.30	-1.51
							Cys 52	3.55	-0.24
21	-104.131	Lys 60	2.69	-2.50	55	-118.004	Cys 57	3.00	-0.64
							Thr 335	3.13	-2.36
							Lys 60	2.98	-1.25
							Try 198	3.49	-0.53
22	-111.561	Lys 60	3.16	-2.19	56	-125.794	Thr 335	2.77	-1.76
								3.04	-2.50
							Thr 51	3.40	-0.57
								2.69	-1.91
23	-118.762	Lys 60	3.02	-1.85	57	-102.122	Cys 52	3.14	-0.98
							Thr 335	3.12	-2.42
							Cys 57	3.00	-0.64
							Lys 60	2.69	-1.36
24	-118.061	Ser 14	2.97	-2.50	58	-102.453	Lys 60	3.10	-2.08
		Thr 335	2.21	0.76				2.90	-1.53

			3.18	-2.11					
		Ser 162	3.17	-1.77				2.80	-1.98
		Arg 287	3.05	-2.04					
25	-116.771	Lys 60	3.57	-0.13	59	-105.655	Lys 60	2.36	-0.47
							Try 198	3.46	-0.39
26	-118.707	Lys 60	3.08	-2.00	60	-107.908	Lys 60	2.79	-1.82
								2.65	-1.77
27	-94.284	Lys 60	2.71	-0.51	61	-112.204	Thr 335	3.07	-2.50
								2.96	-1.03
							Lys 60	2.37	-0.44
							Tyr 198	3.57	-0.16
28	-107.867	Ser 14	2.57	-2.23	62	-121.668	Thr 335	3.15	-2.25
		Thr 335	2.57	-1.89			Thr 51	3.19	1.07
			3.11	-1.90				2.63	-1.85
			2.97	-2.50					
		Arg 287	3.07	-2.16			Cys 52	3.24	-0.71
		Ser 162	3.60	0					
			3.08	-2.08					
29	-113.613	Ser 14	2.88	-2.50	63	-145.502	Lys 60	2.80	-2.06
		Cys 52	3.16	-2.19			Cys 52	3.10	-1.07
								3.34	-1.18
		Lys 60	3.51	-0.44			Thr 335	3.50	-0.19
30	-108.388	Ser 14	2.57	-2.27	64	-155.221	Lys 60	2.53	-1.26
		Tyr 198	3.45	-0.76			Cys 52	3.09	-0.83
		Lys 60	3.37	-0.49				3.23	-1.53
		Thr 335	2.57	-1.87			Thr 335	3.24	-0.54
			2.97	-2.50					
		Arg 287	3.05	-2.13			Ser 14	3.54	-0.30
		Ser 162	3.11	-2.07					
31	-115.255	Ser 14	2.57	-2.22	65	-158.024	Lys 60	3.02	-2.26
		Thr 335	2.57	-1.88			Cys 52	3.08	-2.37
			3.09	-1.91				3.03	-1.04
			2.97	-2.50			Thr 335	3.14	-0.69
		Arg 287	3.07	-2.15			Ser 14	3.35	-1.27
		Ser 162	3.09	-2.09					
32	-115.011	Ser 14	3.45	-0.73	66	-147.809	Lys 60	2.18	-1.93
		Cys 52	3.08	-2.50			Cys 52	3.11	-1.13
								3.39	-1.03
							Thr 335	3.19	-0.72
							Ser 14	3.37	-1.15
33	-118.296	Ser 14	2.56	-2.19	67	-143.973	Lys 60	3.51	-0.33
		Thr 198	3.22	-1.90			Thr 335	3.07	-1.09

		Thr 335	3.10	-2.50				3.44	-0.11
			3.18	-2.09				3.07	-0.14
		Arg 287	3.19	-2.06			Cys 52	2.98	-0.81
		Ser 162	3.11	-2.44					
			3.09	-2.50					
<b>34</b>	-95.239	Thr 335	3.04	-0.34	<b>68</b>	-151.683	Lys 60	2.59	-1.68
			2.96	-1.89					
			3.01	-0.99			Cys 52	3.38	-0.42



**Table S19.** Results of the docking of naphthoquinone derivatives in the active site of the *LaA* protein.

ID	Energy (kcal/mol)	Hydrogen Bond (HB)			ID	Energy (kcal/mol)	Hydrogen Bond (HB)				
		Residues	Distance (Å)	Force			Residues	Distance (Å)	Force		
1	-81.600	Val 149	3.10	-2.42	35	-90.191	Val 149	2.74	-1.80		
		Thr 148	2.98	-2.50			Ser 150	3.10	-1.06		
		Ser 150	3.48	-0.12			Asn 152	3.26	-1.53		
							Thr 148	2.60 3.10	-2.49 -2.49		
2	-83.661	-	-	-	36	-89.049	Val 149	3.18	-1.63		
							Asn 152	3.12	-1.76		
							Thr 148	2.60 3.39	-2.50 -0.96		
3	-90.616	-	-	-	37	-82.695	Asp 194	2.63	-2.50		
4	-99.235	Thr 257	3.00	-2.50	38	-88.696	Asp 194	2.60	-1.65		
		Thr 148	2.60	-2.21			Glu 197	3.15	-1.61		
		Val 149	3.21	-1.12			Asp 141	3.04	-1.88		
		Ser 150	2.94	-2.46							
5	-100.881	His 154	3.11	-1.85	39	-82.015	Ala 140	3.45	-0.30		
							Asp 141	3.20	-2.01		
							Ala 192	2.60	-0.66		
							Glu 197	2.58	-0.66		
							Asp 194	2.72	-2.50		
6	-102.105	-	-	-	40	-105.329	Ser 150	3.27	-1.66		
								3.48	-0.60		
								2.82	-1.36		
								2.60	-2.50		
								2.60	-2.43		
							Thr 148	3.43	-0.85		
								2.41	-0.84		
							Asn 143	3.32	-0.03		
								2.87	-0.10		
							Val 149	2.89	-2.50		
							Asp 194	2.60	-1.25		
							Asp 141	3.33	-0.99		
7	-100.978	Thr 148	3.14	-2.29	41	-108.543	Val 149	3.08	-2.39		
								2.60	-2.50		
		Asn 143	2.60	-2.50			Ser 150	3.36	-1.20		
								3.29	-1.53		
								2.60	-2.50		
		Ser 150	2.56	-1.97			Thr 148	3.27	-1.67		
								2.34	-0.30		
							Glu 197	3.10	-1.67		
							Asp 194	2.65	-0.24		
	3.27	-0.25									

							Asp 141	3.07	-1.72
8	-83.514	Ser 150	3.10	-2.50	42	-94.784	Thr 257	3.32	-1.38
			2.58	-1.67			Ser 150	3.00	-0.68
		Val 149	3.39	-0.77			Thr 148	2.77	-2.50
							3.27	-0.85	
		Thr 148	3.12	-2.40			Asn 152	3.35	-0.70
							Val 149	3.10	-2.18
9	-89.104	Thr 148	3.01	-2.50	43	-111.305	Ser 150	2.96	-2.21
								2.60	-2.30
								2.60	-2.50
								3.29	-1.57
								3.47	-0.65
		Asn 143	2.61	-2.49			Gly 151	3.55	-0.22
							Thr 148	3.34	-1.29
								2.31	-0.10
							Val 149	2.87	-2.50
							Asp 194	2.91	-1.10
Val 149	3.22	-1.81	Asp 141	3.10	-1.60				
10	-85.563	Ser 150	2.86	-1.68	44	-75.88	Ser 150	3.39	-1.07
		Asp 141	3.14	-1.47			Val 149	2.87	-2.5
							Asn 143	3.1	-2.5
								3.1	-2.5
								3.2	-1.98
11	-81.801	-	-	-	45	-86.191	Asn 143	2.86	-2.01
12	-85.155	Asn 143	2.86	-0.50	46	-81.159	Asn 152	3.19	-0.92
		Thr 148	2.91	-2.50					
13	-89.131	Thr 148	2.90	-2.33	47	-85.875	Thr 148	3.36	-1.22
							Asn 143	2.7	-1.08
							Thr 257	3.04	-2.5
14	-101.370	Ser 150	2.95	-1.51	48	-94.363	Val 149	2.63	-2.50
			3.30	-1.48			Ser 150	3.03	-1.00
			3.38	-1.12					
			2.62	-2.26					
			2.51	-1.79					
		Thr 148	3.30	-1.51			Thr 148	3.11	-2.46
		Gly 151	3.52	-0.34					
		Val 149	2.96	-2.44					
		Asp 141	3.11	-1.58					

15	-91.161	Thr 257	3.10	-2.50	49	-86.276	Asp 141	3.10	-2.49		
							Ala 140	3.48	-0.22		
							Glu 197	2.44	-0.59		
							Asp 194	2.65	-0.33		
16	-91.305	Asn 143	2.60	-0.34	50	-96.301	Asp 194	3.56	-0.001		
		Thr 148	3.08	-2.50				3.58	-0.01		
		Thr 257	2.90	-2.50				2.60	-2.50		
		Ser 150	2.46	-1.09			Ala 192	3.10	-2.50		
17	-105.910	Asn 143	3.20	-0.23	51	-90.319	His 139	3.14	-2.29		
			3.11	-1.20							
		Ser 150	3.02	-2.50							
		His 139	2.73	-0.02							
		Thr 257	3.10	-2.39							
18	-85.587	Thr 143	3.06	-2.50	52	-96.058	Thr 148	2.97	-2.50		
				3.11				-2.06			
		Val 149	3.09	-2.50			Asn 152	3.53	-0.34		
		Ser 150	2.60	-2.47			Val 149	2.97	-2.48		
Ser 150	2.60				-2.50						
						Asn 143	2.68	-2.50			
19	-85.055	-	-	-	53	-83.897	Asp 141	3.05	-1.82		
							Glu 197	3.13	-0.47		
							Asp 194	2.6	-1.41		
20	-82.806	-	-	-	54	-89.613	Thr 148	2.6	-2.06		
							Asn 152	2.78	-1.58		
							Ser 150	3.35	-0.08		
21	-84.880	-	-	-	55	-87.163	Thr 148	2.6	-2.5		
							Asn 143	2.6	-0.16		
							Asn 152	2.86	-0.03		
							His 154	3.5	-0.19		
22	-92.461	-	-	-	56	-94.045	Thr 148	2.98	-2.1		
							His 154	3.46	-0.71		
							Asn 152	3.2	-2.01		
23	-84.315	Asn 143	3.10	-2.44	57	-67.630	Ser 150	3.13	-2.27		
		Ser 150	2.41	-0.04			Asn 143	3.35	-0.57		
24	-97.226	Asn 143	3.22	-1.58	58	-86.668	Asn 143	2.94	-1.58		
25	-89.138	-	-	-	59	-71.623	Asn 152	3.24	-1.42		
							Ser 150	3.25	-0.53		
								2.82	-2.50		
							Thr 257	3.46	-0.67		
26	-99.623	Ser 150	3.12	-2.38	60	-76.008	Asn 143	2.88	-0.54		
			2.41	-0.71							
		Val 149	3.47	-0.42							
		Thr 148	2.94	-2.29							
27	-85.381	Asp 141	3.09	-2.03	61	-71.498	Val 149	2.64	-2.40		
		Glu 197	3.36	-1.03			Thr 148	3.34	-1.29		

							Asn 143	2.71	-0.07
							Ser 150	3.20	-2.02
								3.44	-0.35
28	-87.716	Asp 141	3.07	-1.72	62	-83.099	Thr 148	3.47	-0.63
		Glu 197	3.14	-0.92			Asn 143	3.10	-0.84
		Asp 194	2.60	-2.42					
29	-99.351	Val 149	3.00	-1.95	63	-104.823	Asn 143	3.10	-0.81
		Thr 148	2.74	-2.50			Ser 150	3.33	-0.11
								3.11	-2.21
								3.20	-2.01
		3.01	-2.50						
		Ser 150	3.29	-1.53			Thr 148	2.90	-1.68
								2.33	-0.14
		Asp 141	3.05	-1.74			Val 149	2.62	-2.50
		Glu 197	3.07	-1.19					
		Asp 194	2.65	-2.49					
30	-88.975	Asn 143	2.60	-0.23	64	-116.708	Ser 150	2.60	-1.12
		Thr 148	3.00	-2.50				3.24	-1.63
								3.39	-1.03
								2.86	-2.50
							3.39	-0.52	
		Ser 150	2.40	-0.56			Thr 148	3.14	-0.15
								3.05	-0.11
		Val 149	2.60	-2.50					
			2.60	-1.41					
		31	-90.099	Asp 194			2.90	-2.50	65
Ala 192	3.10			-2.48	Thr 148	3.33	-0.14		
						2.79	-2.50		
					2.09	1.81			
					Asn 143	3.48	-0.07		
3.10	-0.38								
Val 149	2.67			-2.02					
	3.40			-0.54					
Ser 150	3.10			-2.50					
	3.10			-2.50					
	3.53	-0.36							
32	-10.517	Thr 257	3.44	-0.80	66	-121.516	Asn 152	3.08	-2.50
		Ser 150	3.53	-0.01			Thr 148	3.10	-0.43
								1.99	2.74
								3.52	-0.38
		2.54	-1.95						
Thr 148	3.10	-2.50	Val 149	3.15	-0.15				

									2.61	-1.18
								3.34	-1.31	
			2.90	-1.66				Ser 150	2.80	-2.50
									3.10	-1.51
									2.16	1.26
		2.49					-1.57			
Val 149	2.60	-2.49	Gly 151	3.22	-1.32					
33	-10.459	Val 149	2.63	-2.50	67	-115.454	Ser 150	3.36	-1.20	
								3.04	-2.15	
								3.10	-2.50	
								2.81	-1.15	
		Ser 150	2.88	-1.71			Thr 148	2.66	-2.50	
								2.46	-0.80	
		Thr 148	2.87	-1.22			Asn 143	3.32	-0.11	
								3.16	-0.87	
		Val 149	3.10	-1.85						
		34	-82.222	Thr 148			2.99	-2.17	68	-112.983
His 154	3.29			-1.53	Thr 148	2.60	-2.50			
Asn 152	3.10			-2.50	Asn 152	3.42	-0.87			
						2.50	-1.65			
						2.97	-2.50			
					Ser 150	3.01	-2.50			
2.89	-2.50									
3.52	-0.39									

**Table S20.** Results of the docking of naphthoquinone derivatives in the active site of the *LiTA* protein.

ID	Energy (kcal/mol)	Hydrogen bond (HB)			ID	Energy (kcal/mol)	Hydrogen bond (HB)		
		Residues	Distance (Å)	Force			Residues	Distance (Å)	Force
1	-79.606	Tyr 256	2.96	-2.50	35	-82.252	Tyr 256	2.18	1.05
			2.79	-0.74			Asn 225	3.10	-2.29
2	-85.849	Asn 225	2.90	-1.44	36	-80.826	Tyr 256	3.01	-2.50
		Gly 79	3.46	-0.39				2.95	-2.50
3	-86.939	Tyr 256	3.00	-1.42	37	-82.337	Tyr 256	2.93	-2.50
								2.86	-2.50
4	-87.891	Tyr 256	3.03	-2.50	38	-81.804	Tyr 256	2.73	-2.50
			3.02	-2.50				2.94	-2.50
5	-92.143	Tyr 256	2.74	-2.50	39	-83.067	Tyr 256	3.01	-2.50
			3.08	-2.50				2.94	-2.50
6	-95.046	-	-	-	40	-84.225	Tyr 256	2.60	-2.50
								3.30	-1.48
								3.12	-2.40
							Asn 225	3.36	-1.19
								2.43	-1.12
7	-90.656	Tyr 256	3.10	-2.50	41	-79.365	Tyr 256	2.67	-2.50
			2.94	-2.50			Asn 225	3.50	-0.24
8	-84.381	Tyr 256	2.99	-2.50	42	-96.985	Asn 225	3.31	-0.61
			2.89	-2.50				3.10	-1.32
9	-89.649	Tyr 256	3.10	-2.34	43	-74.541	Asn 225		
		Asn 225	2.19	0.93				2.60	-2.49
								3.02	-0.05
							Gly 79	3.16	-2.19
								2.60	-2.50
							Tyr 256	3.02	-0.93
10	-84.295	Tyr 256	2.92	-2.50	44	-83.134	Tyr 256	3.1	-2.5
			3.07	-2.50					
11	-84.611	Tyr 256	2.95	-2.50	45	-78.98	Tyr 256	2.95	-2.5
			2.87	-2.50				2.74	-2.5
12	-83.999	Tyr 256	2.85	-2.50	46	-81.058	Asn 256	2.96	-1.43
			2.96	-2.50					
13	-83.373	Asn 225	3.01	-1.50	47	-88.304	-	-	-
14	-87.445	Tyr 256	2.95	-2.50	48	-82.930	Tyr 256	2.99	-2.49
			2.84	-2.50					
15	-94.888	Tyr 256	2.93	-2.50	49	-84.899	Asn 225	3.00	-1.43
			2.79	-2.50					
16	-88.165	Tyr 256	3.03	-2.50	50	-94.022	Gly 79	2.75	-0.69
			2.99	-2.50				2.63	-0.57
17	-94.674	Asn 225	3.14	-1.27	51	-87.735	Tyr 256	2.71	-1.57
		Gly 79	3.43	-0.50					

18	-80.138	Tyr 256	3.07	-2.50	52	-66.356	Tyr 256	2.98	-2.50
			2.91	-1.79				3.02	-2.50
19	-87.227	Tyr 256				-74.986	Tyr 256	3.1	-0.88
			2.94	-2.50				2.86	-2.5
			2.78	-2.50				2.89	-0.31
20	-85.218	Tyr 256				-77.535 -81.348	Tyr 256 Asn 225	3.1	-0.29
			3.03	-2.50				2.69	-2.5
			2.98	-2.50				3.12	-2.42
21	-91.061	Tyr 256					Tyr 256	2.69	-0.72
			3.04	-2.50				2.6	-2.5
			2.77	-0.92				3.08	-2.5
22	-89.106	Tyr 256				-66.914	Tyr 256	2.65	-1.19
			2.94	-2.50				3.12	-2.41
			2.79	-1.01					
23	-85.104	Asn 225	3.10	-1.40	57	-66.913	-	-	-
		Gly 79	3.43	-0.43					
24	-83.580	Tyr 256	3.11	-2.44	58	-69.657	Tyr 256	3.16	-2.18
								2.75	-1.29
25	-96.427	Asn 225	3.06	-1.87	59	-70.068	Tyr 256	2.87	-2.50
								3.09	-0.04
								3.15	-2.25
26	-87.100	-	-	-	60	-76.338	Tyr 256	2.80	-1.20
								2.89	-2.50
27	-86.191	-	-	-	61	-72.644	Tyr 256	3.07	-0.13
28	-85.924	Tyr 256	2.92	-2.50	62	-78.314	Tyr 256	3.08	-2.50
			2.88	-2.50					
29	-84.210	Tyr 256	2.74	-0.14	63	-109.969	Asn 225	3.12	-1.78
								3.44	-0.78
								3.28	-1.58
							Tyr 256	2.97	-2.50
								3.07	-2.50
30	-89.359	Tyr 256	3.00	-2.50	64	-119.504	Tyr 256	2.98	-2.45
			3.01	-2.50					
31	-95.517	Tyr 256	2.77	-2.50	65	-108.703	Gly 79	2.71	-2.71
								2.84	-1.70
								2.68	-2.50
			3.10	-2.50			Tyr 256	3.10	-2.49
32	-87.559	Tyr 256	2.96	-2.50	66	-108.761		3.28	-1.60
								2.70	-2.50
							Tyr 256	3.14	-2.21
			2.73	-2.50			Asn 225	3.01	-1.66
33	-80.096	Tyr 256	3.02	-2.50	67	-121.426	Tyr 256	3.08	-2.50
			3.01	-2.50				3.00	-2.46
34	-87.434	Try 256	2.98	-2.50	68	-113.611	Asn 225	3.12	-1.65
								3.23	-1.85
								2.87	-2.50
			2.82	-2.50			Tyr 256	3.17	-1.91

Table S21. ADME parameters

ID	MW	H-bond acceptors	H-bond donors	TPSA	Pharmacokinetics															Bio- availability Score			
					Solubility (Log S)					GI	Pgp	CYP					log Kp (cm/s)	Lipinski	Ghose		Veber	Egan	Muegge
					Log P				1A2			2C19	2C9	2D6	3A4								
						ESOL	Ali	Silicos- IT															
1	283.71	2	1	46.17	3.06	-4.57	-4.9	-6.43	High	No	Yes	Yes	Yes	Yes	Yes	-5.03	0	0	0	0	0	0.55	
2	313.74	3	1	55.4	3.07	-4.63	-5.06	-6.55	High	No	Yes	Yes	Yes	Yes	Yes	-5.24	0	0	0	0	0	0.55	
3	313.74	3	1	55.4	3.05	-4.63	-5.06	-6.55	High	No	Yes	Yes	Yes	Yes	Yes	-5.24	0	0	0	0	0	0.55	
4	313.74	3	1	55.4	3.05	-4.63	-5.06	-6.55	High	No	Yes	Yes	Yes	Yes	Yes	-5.24	0	0	0	0	0	0.55	
5	327.76	3	1	55.4	3.4	-4.87	-5.45	-6.95	High	No	Yes	Yes	Yes	Yes	Yes	-5.06	0	0	0	0	0	0.55	
6	326.77	3	0	43.37	3.9	-4.86	-5.19	-7.3	High	No	Yes	Yes	Yes	Yes	Yes	-5.06	0	0	0	0	0	0.55	
7	327.76	3	1	55.4	3.38	-4.87	-5.45	-6.95	High	No	Yes	Yes	Yes	Yes	Yes	-5.06	0	0	0	0	0	0.55	
8	301.7	3	1	46.17	3.41	-4.72	-5	-6.71	High	No	Yes	Yes	Yes	Yes	Yes	-5.07	0	0	0	0	0	0.55	
9	301.7	3	1	46.17	3.38	-4.72	-5	-6.71	High	No	Yes	Yes	Yes	Yes	Yes	-5.07	0	0	0	0	0	0.55	
10	301.7	3	1	46.17	3.38	-4.72	-5	-6.71	High	No	Yes	Yes	Yes	Yes	Yes	-5.07	0	0	0	0	0	0.55	
11	318.15	2	1	46.17	3.62	-5.16	-5.55	-7.04	High	No	Yes	Yes	Yes	No	Yes	-4.8	0	0	0	0	0	0.55	
12	318.15	2	1	46.17	3.62	-5.16	-5.55	-7.04	High	No	Yes	Yes	Yes	No	Yes	-4.8	0	0	0	0	0	0.55	
13	318.15	2	1	46.17	3.6	-5.16	-5.55	-7.04	High	No	Yes	Yes	Yes	No	Yes	-4.8	0	0	0	0	0	0.55	
14	328.71	4	1	91.99	2.47	-4.96	-6.26	-5.79	High	No	Yes	Yes	Yes	No	Yes	-5.04	0	0	0	0	0	0.55	
15	328.71	4	1	91.99	2.3	-4.62	-5.69	-5.79	High	No	Yes	Yes	Yes	No	Yes	-5.43	0	0	0	0	0	0.55	
16	328.71	4	1	91.99	2.3	-4.62	-5.69	-5.79	High	No	Yes	Yes	Yes	No	Yes	-5.43	0	0	0	0	0	0.55	
17	373.7	6	1	137.81	1.68	-5.03	-7.04	-5.14	Low	No	Yes	Yes	Yes	Yes	Yes	-5.43	0	0	0	1	0	0.55	
18	297.74	2	1	46.17	3.41	-4.86	-5.27	-6.82	High	No	Yes	Yes	Yes	Yes	Yes	-4.86	0	0	0	0	0	0.55	
19	297.74	2	1	46.17	3.42	-4.86	-5.27	-6.82	High	No	Yes	Yes	Yes	Yes	Yes	-4.86	0	0	0	0	0	0.55	
20	297.74	2	1	46.17	3.4	-4.86	-5.27	-6.82	High	No	Yes	Yes	Yes	Yes	Yes	-4.86	0	0	0	0	0	0.55	
21	311.76	2	1	46.17	3.7	-5.14	-5.73	-7.21	High	No	Yes	Yes	Yes	Yes	Yes	-4.64	0	0	0	0	1	0.55	
22	311.76	2	1	46.17	3.7	-5.14	-5.73	-7.21	High	No	Yes	Yes	Yes	Yes	Yes	-4.64	0	0	0	0	1	0.55	
23	311.76	2	1	46.17	3.7	-5.14	-5.73	-7.21	High	No	Yes	Yes	Yes	Yes	Yes	-4.64	0	0	0	0	1	0.55	
24	325.79	2	1	46.17	4.01	-5.42	-6.07	-7.24	High	No	Yes	Yes	Yes	No	Yes	-4.49	0	0	0	0	1	0.55	
25	325.79	2	1	46.17	4.02	-5.42	-6.07	-7.24	High	No	Yes	Yes	Yes	No	Yes	-4.49	0	0	0	0	1	0.55	



26	325.79	2	1	46.17	4.01	-5.42	-6.07	-7.24	High	No	Yes	Yes	Yes	No	Yes	-4.49	0	0	0	0	1	0.55
27	264.28	2	2	72.19	2.05	-3.62	-4.09	-5.47	High	No	Yes	Yes	Yes	No	Yes	-5.85	0	0	0	0	0	0.55
28	294.3	3	2	81.42	1.95	-3.57	-4.06	-5.58	High	No	Yes	Yes	Yes	No	Yes	-6.18	0	0	0	0	0	0.55
29	294.3	3	2	81.42	1.94	-3.68	-4.25	-5.58	High	No	Yes	Yes	Yes	No	Yes	-6.05	0	0	0	0	0	0.55
30	294.3	3	2	81.42	1.95	-3.68	-4.25	-5.58	High	No	Yes	Yes	Yes	No	Yes	-6.05	0	0	0	0	0	0.55
31	308.33	3	2	81.42	2.26	-3.81	-4.45	-5.98	High	No	Yes	Yes	Yes	Yes	Yes	-6	0	0	0	0	0	0.55
32	308.33	3	2	81.42	2.23	-3.92	-4.63	-5.98	High	No	Yes	Yes	Yes	Yes	Yes	-5.87	0	0	0	0	0	0.55
33	308.33	3	2	81.42	2.27	-3.92	-4.63	-5.98	High	No	Yes	Yes	Yes	Yes	Yes	-5.87	0	0	0	0	0	0.55
34	282.27	3	2	72.19	2.28	-3.78	-4.19	-5.74	High	No	Yes	No	No	Yes	Yes	-5.88	0	0	0	0	0	0.55
35	282.27	3	2	72.19	2.26	-3.78	-4.19	-5.74	High	No	Yes	No	No	Yes	Yes	-5.88	0	0	0	0	0	0.55
36	282.27	3	2	72.19	2.25	-3.78	-4.19	-5.74	High	No	Yes	No	No	Yes	Yes	-5.88	0	0	0	0	0	0.55
37	298.72	2	2	72.19	2.49	-4.21	-4.74	-6.07	High	No	Yes	Yes	Yes	Yes	Yes	-5.61	0	0	0	0	0	0.55
38	298.72	2	2	72.19	2.49	-4.21	-4.74	-6.07	High	No	Yes	Yes	Yes	Yes	Yes	-5.61	0	0	0	0	0	0.55
39	298.72	2	2	72.19	2.48	-4.21	-4.74	-6.07	High	No	Yes	Yes	Yes	Yes	Yes	-5.61	0	0	0	0	0	0.55
40	309.28	4	2	118.01	1.27	-3.9	-5.26	-4.83	High	No	Yes	No	Yes	No	Yes	-5.98	0	0	0	0	0	0.55
41	309.28	4	2	118.01	1.22	-3.67	-4.87	-4.83	High	No	Yes	No	Yes	No	Yes	-6.24	0	0	0	0	0	0.55
42	309.28	4	2	118.01	1.2	-3.67	-4.87	-4.83	High	No	Yes	No	Yes	No	Yes	-6.24	0	0	0	0	0	0.55
43	354.27	6	2	163.83	0.49	-3.97	-6.04	-4.18	Low	No	No	No	Yes	No	Yes	-6.37	0	0	1	1	1	0.55
44	292.33	2	2	72.19	2.57	-4.2	-4.92	-6.25	High	No	Yes	Yes	Yes	Yes	Yes	-5.45	0	0	0	0	0	0.55
45	306.36	2	2	72.19	2.86	-4.36	-5.07	-6.27	High	No	Yes	Yes	Yes	Yes	Yes	-5.43	0	0	0	0	0	0.55
46	306.36	2	2	72.19	2.89	-4.47	-5.26	-6.27	High	No	Yes	Yes	Yes	Yes	Yes	-5.3	0	0	0	0	0	0.55
47	306.36	2	2	72.19	2.87	-4.47	-5.26	-6.27	High	No	Yes	Yes	Yes	Yes	Yes	-5.3	0	0	0	0	0	0.55
48	278.31	2	2	72.19	2.26	-3.8	-4.27	-5.85	High	No	Yes	Yes	Yes	Yes	Yes	-5.8	0	0	0	0	0	0.55
49	278.31	2	2	72.19	2.29	-3.92	-4.47	-5.85	High	No	Yes	Yes	Yes	Yes	Yes	-5.67	0	0	0	0	0	0.55
50	278.31	2	2	72.19	2.28	-3.92	-4.47	-5.85	High	No	Yes	Yes	Yes	Yes	Yes	-5.67	0	0	0	0	0	0.55
51	292.33	2	2	72.19	2.56	-4.08	-4.73	-6.25	High	No	Yes	Yes	Yes	Yes	Yes	-5.58	0	0	0	0	0	0.55
52	292.33	2	2	72.19	2.58	-4.2	-4.92	-6.25	High	No	Yes	Yes	Yes	Yes	Yes	-5.45	0	0	0	0	0	0.55
53	290.27	5	0	69.15	2.21	-3.87	-3.9	-6.29	High	No	Yes	No	Yes	Yes	Yes	-6.09	0	0	0	0	0	0.55
54	290.27	5	0	69.15	2.25	-3.87	-3.9	-6.29	High	No	Yes	No	Yes	Yes	Yes	-6.09	0	0	0	0	0	0.55
55	304.3	5	0	69.15	2.55	-4.1	-4.28	-6.69	High	No	Yes	No	Yes	No	Yes	-5.91	0	0	0	0	0	0.55
56	304.3	5	0	69.15	2.56	-4.1	-4.28	-6.69	High	No	Yes	No	Yes	No	Yes	-5.91	0	0	0	0	0	0.55
57	274.27	4	0	59.92	2.59	-4.11	-4.11	-6.56	High	No	Yes	No	No	No	Yes	-5.72	0	0	0	0	0	0.55
58	274.27	4	0	59.92	2.62	-4.11	-4.11	-6.56	High	No	Yes	No	Yes	No	Yes	-5.72	0	0	0	0	0	0.55
59	288.3	4	0	59.92	2.88	-4.38	-4.57	-6.96	High	No	Yes	Yes	Yes	No	Yes	-5.49	0	0	0	0	0	0.55

60	288.3	4	0	59.92	2.88	-4.38	-4.57	-6.96	High	No	Yes	Yes	Yes	No	Yes	-5.49	0	0	0	0	0	0.55
61	302.33	4	0	59.92	3.19	-4.65	-4.91	-6.99	High	No	Yes	Yes	Yes	No	Yes	-5.34	0	0	0	0	0	0.55
62	302.33	4	0	59.92	3.19	-4.65	-4.91	-6.99	High	No	Yes	Yes	Yes	No	Yes	-5.34	0	0	0	0	0	0.55
63	364.79	4	1	76.88	2.65	-4.49	-4.74	-6.95	High	No	Yes	Yes	Yes	No	Yes	-6.08	0	0	0	0	0	0.55
64	382.78	5	1	76.88	3.01	-4.65	-4.84	-7.22	High	No	Yes	Yes	Yes	No	Yes	-6.12	0	0	0	0	0	0.55
65	382.78	5	1	76.88	3.01	-4.65	-4.84	-7.22	High	No	Yes	Yes	Yes	No	Yes	-6.12	0	0	0	0	0	0.55
66	382.78	5	1	76.88	2.98	-4.65	-4.84	-7.22	High	No	Yes	Yes	Yes	No	Yes	-6.12	0	0	0	0	0	0.55
67	400.77	6	1	76.88	3.3	-4.8	-4.94	-7.48	High	No	Yes	Yes	Yes	No	Yes	-6.16	0	0	0	0	0	0.55
68	400.77	6	1	76.88	3.28	-4.8	-4.94	-7.48	High	No	Yes	Yes	Yes	No	Yes	-6.16	0	0	0	0	0	0.55