SUPPORTING INFORMATION

Ligand-Based Virtual Screening and *in silico* Design of New Antimalarial Compounds Using Non-Stochastic and Stochastic Total and Atom-type Quadratic Maps

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Table 5. Classification of Active Compounds in the Training and Test Sets by the Use of LDA-QSAR Models Developed Using Non-stochastic (Eq. 11) and Stochastic (Eq. 12) Quadratic Indices.

name ^a	$\Delta P\%^b$	$\Delta P\%^c$	name ^a	$\Delta P\%^b$	$\Delta P\%^c$
Training Active Group					
Cinchonine	-78.57	-82.98	21	99.51	97.25
Hydroxychloroquine	59.02	62.34	22	99.80	99.25
CDRI 87209	-24.92	-49.49	23	99.58	98.53
WR 33,063	99.99	99.98	24	99.15	97.41
WR 122,455	23.30	31.60	25	99.81	99.30
Pamaquine	80.67	69.16	27	99.43	97.76
Primaquine	-60.69	-11.63	Benzonaphthyridine 7351	99.96	99.59
WR 225498	93.61	98.23	28	89.19	55.96
WR 242511	95.01	98.80	30	87.92	78.59
M8506,Trifluoracetylprimaquine	80.20	-45.52	32	98.62	95.38
CDRI 8053	91.76	92.46	12278 R	99.04	99.29
Chloroguanide	-69.10	-17.19	34	99.05	91.65
Chloroproguanil	-43.29	44.10	Secoartemisinin	98.73	96.47
Pyrimetamine	74.18	9.71	(+)- 4,5 Secoartemisinin	98.72	96.07
Trimethoprim	61.92	-14.10	36	97.28	90.48
Sulfalene	42.84	1.08	9- Desmethylartemisinin	86.42	71.90
Dapsone	-95.59	-49.40	38	96.82	94.96
Sulfisoxazole	89.26	76.08	39	96.86	95.56
WR 99210	91.41	96.91	40	98.52	97.72
PS-15	80.75	97.82	42	99.31	98.82
Artemisinin	96.84	94.52	43	99.68	99.39
Bispyroquine	98.93	92.18	44	100.00	100.00
Fluornemethanol	91.18	99.06	46	93.61	76.93
Artemisitene	92.24	90.38	47	96.35	91.84
1	96.28	95.98	6,9 Didesmethylartemisinin	86.42	71.90
B-artether	99.46	98.20	49	98.76	97.63
2	99.46	98.20	50	99.42	98.78
3	98.41	93.25	51	99.59	99.00
Sodium artesunate	99.69	97.85	53	99.97	99.93
4	99.92	99.39	54	99.98	99.94
Tripiperakin	90.09	92.22	55	98.43	86.20
6	99.80	99.84	56	67.86	57.39
7	100.00	99.97	58	-3.51	-34.71
9	100.00	100.00	59	-12.31	7.31
10	99.74	99.89	60	96.84	94.52
11	99.87	99.72	61	97.41	95.21
13	99.97	99.85	62	94.82	86.91
14	99.61	98.32	64	99.66	99.22
6-demethyl-6-difluoromethyl B-artether	99.87	99.86	65	98.04	96.57
15	96.82	89.50	66	99.96	99.78
17	99.93	99.49	67	100.00	99.99
Gossypol	100.00	99.99	69	99.13	94.98
CN 10443	99.97	99.99	70	99.82	99.19
19	94.71	78.19	Lapinone	99.97	99.99

Table 5. Cont.

name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c	name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c
Mencitone	96.42	98.73	Amquinat	49.39	80.70
Pyronaridine	99.89	98.90	Fluoroquine	82.84	94.42
Quinacrine	97.88	96.80	Pentaquine	53.60	62.85
Amodiaquine	93.93	80.55	Dabekhin	-36.27	-45.54
Tetracycline	95.35	93.96	Methylchloroquine	90.61	90.15
Doxycycline	89.78	93.53	RC- 12	73.00	80.52
Clindamycin	87.13	99.86	Dimeplasmin	52.84	50.33
Ciprofloxacin	-97.92	21.69	Azamepacrine	98.96	98.75
Yingzhaosu A	98.50	94.47	Mepacrine	98.00	96.87
Yingzhaosu C	89.38	74.08	Aristochin	99.44	99.33
Arteflene	97.45	90.05	85	-71.82	49.28
Fenozan - 50 F	98.23	99.86	87	-48.74	83.75
71	99.96	99.70	88	-32.86	94.05
Exifone	77.75	62.00	89	7.74	97.73
Methylene blue	-99.46	-97.79	91	-46.42	90.73
WR 197236	32.16	94.63	Chalcone	-94.93	-37.68
Piperaquine	59.26	86.15	93	76.68	72.17
Desferrioxamine	100.00	99.88	95	84.78	84.98
73	20.65	97.49	96	27.28	36.77
74	100.00	100.00	98	96.48	95.76
76	99.91	99.98	100	99.22	98.85
77	-94.93	-37.68	101	74.79	63.20
78	37.64	65.03	102	20.16	8.58
Axisonitrile-3	-43.14	-26.20	104	99.95	99.73
Berbamine	96.19	98.80	105	99.82	99.60
Malagashanine	-68.27	-59.53	107	99.10	97.92
Berberine	-98.70	-76.10	108	99.80	99.44
10,12 Peroxycalamenene	85.32	71.56	109	99.41	99.73
Simalikalactone D	97.75	99.40	111	96.94	92.76
Gutolactone	94.41	98.02	112	99.75	99.88
Lissoclinotoxin A	96.94	30.43	114	47.17	16.46
Licochalcone A	0.51	47.43	115	52.93	46.97
80	-68.79	-66.99	117	82.38	64.15
82	53.09	78.94	118	97.89	86.49
Cycloleucine	-99.68	-98.48	119	93.97	86.23
Nitroguanil	14.31	0.64	120	93.97	86.23
Cloguanamil	-99.30	-90.26	2-(4-Metoxibenzoyl)-1-naphthoil acid	-97.58	-93.39
Metachloridine	42.22	14.50	Oxalic bis(2-hidroxy-1-naphthylmethylene)hidrazide	62.88	-29.90
Supazine	29.66	-88.95	122	88.04	94.51
Cilional	6.30	-60.17	123	94.17	97.32
WR 10 488	-38.75	82.47	124	99.80	99.92
Acedapsone	-81.07	-16.01	125	99.91	99.96
Gentiopiecrim	-96.18	-23.70	127	99.52	99.80
Oxychlorochin	-2.11	20.35	Buquinolate	98.79	99.67
Antimalarine	17.84	6.79	Decoquinat	99.89	99.97
Brindoxime	62.86	91.65	Methyl benzoquate	66.51	85.73

Table 5. Cont.

name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c	name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c
129	95.56	99.73	198	99.98	99.52
130	99.39	99.98	199	99.74	86.16
132	97.75	98.70	200	98.99	98.06
133	98.13	99.10	202	99.24	98.36
135	99.59	99.80	203	99.66	99.22
136	93.93	96.73	204	99.39	98.95
138	96.30	94.60	206	97.41	95.21
139	93.52	96.99	207	99.81	99.62
140	77.16	-10.48	208	98.04	96.57
142	88.96	97.24	209	39.07	37.12
144	99.42	94.41	210	66.06	61.91
146	99.79	98.93	211	82.59	78.36
147	96.43	38.38	213	16.90	-33.73
148	97.38	45.26	214	-33.42	-73.97
150	97.64	59.61	216	93.08	62.92
152	92.52	19.03	217	9.20	-14.27
153	93.93	80.55	219	44.10	12.75
155	98.72	98.47	220	69.35	42.47
156	99.89	98.85	221	98.77	97.12
157	99.92	99.75	222	99.35	98.47
159	99.86	99.75	223	99.72	99.73
160	100.00	99.99	224	99.87	99.84
162	62.55	69.90	225	99.50	99.76
163	75.87	99.44	226	99.76	97.81
165	79.43	58.53	227	99.76	97.81
166	99.99	100.00	228	99.91	99.99
167	99.95	100.00	229	99.95	99.68
169	92.03	98.55	230	99.83	99.87
170	99.98	100.00	231	99.85	90.58
171	57.56	-56.76	232	99.85	90.58
173	92.33	54.73	233	99.53	98.42
174	99.21	92.36	234	99.53	98.42
176	83.78	21.00	235	99.85	99.90
177	96.40	74.06	236	99.85	99.89
178	71.92	-28.04	237	99.85	99.89
180	87.24	40.86	238	100.00	100.00
181	72.38	-35.77	239	25.26	-10.30
182	79.90	-17.06	241	73.84	64.94
184	70.82	-10.13	242	86.88	80.21
185	59.95	-18.12	243	53.81	52.29
187	36.95	-51.85	245	94.08	91.72
188	81.32	27.42	246	98.86	98.82
189	99.83	89.37	248	93.53	94.44
191	100.00	98.39	249	95.01	98.68
192	100.00	99.74	250	95.25	93.87
194	99.95	98.53	252	96.95	96.04
195	99.98	95.83	253	90.09	88.46
196	99.99	99.51	255	99.95	99.82

Table 5. Cont.

name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c	name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c
256	86.62	89.51	318	98.85	93.43
257	89.60	97.46	320	100.00	99.99
259	87.92	78.59	321	96.59	99.73
260	97.87	99.77	322	99.94	99.66
261	90.64	88.00	324	99.99	99.97
262	92.98	87.73	325	99.96	99.54
264	95.22	92.62	326	99.96	99.72
265	98.01	93.41	327	99.90	99.03
266	99.46	99.77	330	97.84	87.39
268	97.81	99.35	331	99.85	99.56
269	98.10	94.71	332	99.98	99.94
270	99.98	99.94	333	99.93	99.85
271	99.99	99.99	335	99.30	98.37
272	99.98	99.92	336	99.76	99.17
273	99.98	99.90	337	99.89	99.75
275	99.97	99.94	338	99.98	99.91
276	99.96	99.69	340	99.27	96.95
277	99.97	99.64	341	99.78	98.88
279	75.80	99.20	342	99.80	99.40
280	55.18	96.95	343	99.92	99.62
281	98.46	94.03	345	99.91	99.99
282	98.31	96.01	346	99.93	100.00
284	99.22	93.46	347	99.94	99.99
285	99.67	97.29	348	97.09	91.33
287	99.65	96.62	350	99.26	99.93
288	99.53	96.09	351	93.89	79.52
289	98.90	89.88	352	86.46	49.74
291	-19.07	89.48	353	99.61	98.44
292	92.39	99.39	355	99.72	99.59
293	35.57	99.86	356	99.82	99.38
294	96.82	89.50	357	99.63	97.35
296	100.00	100.00	359	97.09	91.33
297	94.30	84.43	360	99.39	99.35
298	97.28	90.48	362	99.88	99.81
300	89.37	84.27	363	98.40	90.02
301	94.43	82.06	364	99.07	97.20
302	98.75	95.85	366	99.55	97.76
304	99.73	98.89	367	99.96	99.96
305	99.87	99.42	369	99.96	99.25
306	99.76	98.09	370	98.15	91.24
308	97.36	95.38	371	99.78	99.34
309	98.76	97.63	372	99.75	99.20
310	99.42	98.78	374	99.60	98.20
312	99.76	98.92	375	99.91	99.66
313	98.90	96.06	376	92.48	99.40
314	99.75	99.45	378	94.78	99.65
316	97.30	86.66	379	97.41	80.71
317	96.82	89.50	380	99.22	93.46

Table 5. Cont.

name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c	name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c
381	98.97	92.33	423	98.69	96.49
383	100.00	100.00	425	99.71	99.04
384	71.34	89.80	426	99.85	99.85
385	-7.20	-43.10	427	99.97	99.96
386	90.77	88.59	428	99.87	99.76
387	99.02	98.93	430	99.99	99.96
388	42.74	16.00	431	99.98	99.97
390	83.94	71.50	432	-27.37	70.96
391	47.40	34.49	433	91.95	99.08
392	99.96	99.83	434	63.61	93.62
394	91.68	86.61	436	99.15	99.87
396	69.79	50.51	437	100.00	100.00
397	99.97	99.92	438	99.98	99.86
398	82.31	81.45	440	99.99	99.94
400	99.80	99.61	441	98.77	65.99
401	28.94	-34.41	442	99.27	80.60
403	-6.01	71.14	443	99.27	80.60
404	71.34	90.41	445	96.73	74.66
405	47.17	76.94	446	99.45	90.77
407	-87.02	38.69	447	96.73	74.66
408	23.59	-57.69	448	97.98	88.28
409	57.62	-25.69	Aminopterin	99.91	94.73
410	81.05	-3.05	449	100.00	100.00
412	20.66	-53.74	450	100.00	100.00
413	55.52	-20.27	451	100.00	100.00
414	79.97	2.69	452	99.62	99.91
416	100.00	100.00	453	97.71	99.02
12-(3'-hydroxy-n-propyl)- deoxoartemisinin	99.59	98.65	454	98.19	98.83
417	96.84	94.52	456	99.89	99.78
418	96.86	95.88	457	99.21	99.60
419	98.52	97.89	459	99.17	99.44
421	99.30	98.53	460	99.96	99.90
422	99.30	98.53			
Test Active Group					
Quinine	-56.15	-61.41	Iso-artemisiten	95.21	88.86
Chloroquine	77.93	77.96	B-artemether	98.41	93.25
Mefloquine	49.30	42.50	Artelinic acid	99.76	98.31
Halofrantine	93.22	98.16	5	99.81	97.77
Quinocide	-61.12	-4.28	8	99.78	99.70
WR 238,605	97.48	99.34	12	99.46	98.25
WR182393	31.77	80.98	7,7 Difluoro-B-artether	99.87	99.84
Cycloguanil	-87.33	-85.04	16	97.03	88.18
Sulfadoxine	69.93	41.35	18	99.90	83.67
Sulfamethoxazole	71.96	42.99	20	97.35	90.75
Clociguanil	24.93	41.50	Cycloquin	100.00	99.99
Nitroquine	99.76	92.53	26	89.66	81.50
Dihydroartemisinin	96.60	87.33	29	86.46	49.74

Table 5. Cont.

name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c	name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c
31	99.22	93.46	110	99.87	99.93
33	96.83	74.62	113	45.17	-19.31
35	99.77	99.08	116	16.28	59.12
37	97.61	89.77	Naphthol blue-black	100.00	100.00
9-Epiartemisinin	93.39	90.01	121	87.14	98.02
41	98.51	97.21	126	99.99	100.00
45	99.39	97.97	128	99.99	99.98
48	97.36	95.38	131	99.86	99.91
52	99.87	99.73	134	99.77	99.64
Lapacol	-88.44	-45.84	137	90.63	99.65
57	93.03	91.97	141	84.19	5.48
Tebuquine	99.09	95.08	143	98.72	98.47
63	99.81	99.62	145	-64.70	-42.74
Octanoylprimaquine	99.54	98.80	149	97.34	68.64
68	99.86	96.98	151	99.76	94.91
Hydrolapachol	-75.01	6.04	154	45.50	-40.79
Atovaquone	-65.89	-24.04	158	-19.20	-4.31
Amopyroquine	85.72	52.21	161	-1.60	13.24
Azithromycin	100.00	100.00	164	89.66	99.62
Norfloxacin	-98.10	4.63	168	50.93	83.44
Enpiroline	60.93	48.61	172	66.91	-20.95
Refigallol	97.51	92.07	175	85.74	36.93
WR 194905	99.66	99.92	179	26.85	-69.71
72	98.72	98.47	183	92.03	71.09
75	99.95	99.99	186	57.34	-18.38
Dioncophyline B	95.41	74.06	190	99.98	92.75
Strychnobrasiline	-86.33	-90.25	193	99.94	97.87
79	99.76	99.52	197	100.00	100.00
Brusatol	97.48	99.47	201	97.54	95.38
81	-21.85	-13.60	205	99.33	99.11
Hexalorxylol	-93.86	-95.27	212	82.49	71.64
WR 135 403	73.05	-5.14	215	81.93	44.87
WR 226 253	30.63	77.24	218	43.24	48.47
CI - 608	-42.29	99.67	240	51.21	41.69
Endochin	79.02	76.76	244	87.73	84.57
Isopentachin	65.34	69.59	247	97.20	55.46
Floxacrine	24.78	48.64	251	43.55	95.98
Aecachinium	-11.21	15.84	254	8.53	92.37
83	-22.22	19.18	258	95.60	90.81
84	-8.37	72.78	263	95.10	88.31
86	-6.26	91.60	267	95.42	98.56
90	-37.08	96.00	274	99.96	99.76
92	10.60	25.65	278	77.71	98.79
94	45.05	53.26	283	96.49	85.51
97	70.02	72.82	286	99.72	99.59
99	99.83	99.69	290	24.87	98.69
103	24.38	24.74	295	97.42	88.99
106	99.17	98.50	299	98.72	96.07

Table 5. Cont.

name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c	name ^a	$\Delta P\%$ ^b	$\Delta P\%$ ^c
303	99.42	97.85	382	99.99	99.90
307	99.88	99.50	389	68.47	51.02
311	99.42	98.34	393	99.27	96.56
315	99.59	99.00	395	10.04	-10.42
319	99.54	96.22	399	95.86	94.69
323	99.98	99.88	402	50.56	99.18
328	99.70	98.92	406	70.03	84.62
329	93.37	70.29	411	96.92	61.18
334	99.88	99.75	415	99.97	99.99
339	99.36	97.89	420	99.31	98.92
344	99.44	98.67	424	99.71	99.51
349	98.79	93.66	429	99.99	99.98
354	99.22	93.46	435	96.16	99.53
358	99.87	99.84	439	99.93	99.46
361	87.79	69.00	444	98.79	92.67
365	99.57	99.37	Methotrexate	99.54	87.52
368	99.89	99.68	Apicidin	100.00	100.00
373	99.61	98.44	455	99.14	99.44
377	92.58	99.75	458	98.24	98.84

^aCompounds structures represent with numbers are given in Table 5a (see Supporting Information);

^bResults of the classification of compounds obtained from Eq. 11 (using non-stochastic quadratic indices);

^cResults of the classification of compounds obtained from Eq. 12 (using stochastic quadratic indices): $\Delta P\% = [P(\text{Active}) - P(\text{Inactive})] \times 100$; where P(active) is the probability that the equations classify a compound as active. Conversely, P(Inactive) is the probability that the models classify a compound as inactive. This value ($\Delta P\%$) takes positive values when $P(\text{active}) > P(\text{Inactive})$ and negative otherwise. Therefore, when $\Delta P\%$ is positive (negative) the compound was classified as antimalarial (non-antimalarial).

Table 5a. Molecular Structure of Antimalarial Compounds Selected from Literature for Developing the Classification Models.

(1)	(2)	(3)	(4)

(5)	(6)	(7)	(8)

(9)	(10)

(11)	(12)	(13)	(14)

(15)	(16)	(17)	(18)

(19)	(20)	(21)	(22)

(23)	(24)	(25)	(26)

Table 5a. Cont.

(27)	(28)	(29)	(30)

(31)	(32)	(33)	(34)

(35)	(36)	(37)	(38-47)					
no	R	R'	no	R	R'	no	R	R'
38	CH ₃	CH ₃	39	Et	H	40	<i>n</i> -Propyl	H
41	<i>i</i> -Propyl	H	42	<i>n</i> -Butyl	H	43	<i>n</i> -pentyl	H
44	Tetradecyl	H	45	(CH ₂) ₃ Ph		46	CH ₂ COOH	H
47	CH ₂ CHCH ₂	H	48	Me	H	49	Et	H
50	<i>n</i> -Propyl	H	51	EtO ₂ CCH ₂	H	52	Me	<i>n</i> -Butyl
53	<i>n</i> -Propyl	<i>n</i> -Butyl	54	EtO ₂ CCH ₂	<i>n</i> -Butyl

(48-54)	(55)	(56)	(57)

(58)	(59)	(60)	(61-65)					
no	R	R'	no	R	R'	no	R	R'
61	H	CH ₃	62	CH ₃	H	63	<i>i</i> -butyl	CH ₃
64	CH ₂ -(2-pyridyl)	CH ₃	65	CH ₂ CHO	CH ₃			

Table 5a. Cont.

Table 5a. Cont.

no	R	R ₁	R ₂	X	no	R	R ₁	R ₂	X
83	Cl	H	4-ClC ₆ H ₄	S	84	F	H	4-ClC ₆ H ₄	S
85	Cl	CH ₃	C ₆ H ₅	SO ₂	86	Cl	H	2,3-(CH ₃ O) ₂ C ₆ H ₃	SO ₂
87	Cl	H	4-ClC ₆ H ₄	SO ₂	88	F	H	3-CH ₃ OC ₆ H ₄	SO ₂
89	F	H	3,4-(CH ₃ O) ₂ C ₆ H ₃	SO ₂	90	F	H	4-ClC ₆ H ₄	SO ₂
91	F	CH ₃	CH ₃	SO ₂					

	no	X	R	no	X	R
(92-110)	92	Cl	(CH ₂) ₃	93	Br	CHMe(CH ₂) ₃
	94	Cl	(CH ₂) ₄	95	Cl	(CH ₂) ₆
	96	Cl	CHMeCH ₂	97	Cl	(CH ₂) ₅
	98	Cl	(CH ₂) ₈	99	Cl	(CH ₂) ₁₂
	100	Cl	(CH ₂) ₁₀	101	I	CHMe(CH ₂) ₃
	102	I	CHMeCH ₂	103	Br	CHMeCH ₂
	104	CF ₃	(CH ₂) ₁₂	105	Br	(CH ₂) ₁₂
	106	Br	(CH ₂) ₁₀	107	I	(CH ₂) ₁₀
	108	I	(CH ₂) ₁₂	109	F	(CH ₂) ₁₀
	110	F	(CH ₂) ₁₂

(111)	(112)	(113)	(114)
(115)	(116)	(117)	(118)
(119)	(120)	(121-127)	

no	R ₁	R ₂	R ₃	no	R ₁	R ₂	R ₃
121	C ₂ H ₅	<i>n</i> -C ₃ H ₇ -	<i>p</i> -ClC ₆ H ₄ CH ₂ O-	122	CH ₃	<i>n</i> -C ₄ H ₉ -	C ₆ H ₅ OCH ₂ CH ₂ O-
123	CH ₃	<i>n</i> -C ₄ H ₉ -	<i>p</i> -CH ₃ C ₆ H ₄ OCH ₂ CH ₂ O-	124	C ₂ H ₅	<i>n</i> -C ₄ H ₉ -	C ₆ H ₅ O(CH ₂) ₆ O-
125	CH ₃	CH ₂ =CHCH ₂ O-	C ₁₂ H ₂₅ O-	126	C ₂ H ₅	<i>n</i> -C ₃ H ₇ O-	C ₁₂ H ₂₅ O-
127	CH ₃	<i>n</i> -C ₄ H ₉ -	<i>n</i> -C ₈ H ₁₇ O-

(128)

Table 5a. Cont.

Table 5a. Cont.

(139)	(140)	(141)

(142)	(143)

(144)	(145)	(146)							
<hr/>
no	R							
(147-152)	147		no	R					
	149		148
	151		150
			152
<hr/>

(153)	(154)	(155-159)							
<hr/>									
no	R₂	R₃	R₇	R₄					
<hr/>									
155	H	CH	Cl		156	H	CH	CF ₃
157	Ph	N	H		158	H	CH	Cl

Table 5a. Cont.

no	R ₂	R ₃	R ₇	R ₄		
159	H	CH	Cl
(160)

(161)

(162)

(163)

(164)

(165)

AA = D-Valyl (166)						
AA = D-Alanine (167)

X = OH (168)						
X = Alanyl (169)						
X = Alanyl-Leucyl-Alanyl (170)

(171-188)						
no	C _{1'}	C ₆	C ₃	C ₅	C _{2'}	C _{3'}
171	NHCH ₃	H	H	H	H	H
172	N(CH ₂ CH ₃)(CH ₃)	H	H	H	H	H
173	NH(CH ₂) ₂ CH ₃	H	H	H	H	H
174	NH(CH ₂) ₅ CH ₃	H	H	H	H	H
175	NH ₂	Cl	H	H	H	H
176	NHC ₂ H ₅	H	H	H	H	H
177	NH(CH ₂) ₃ CH ₃	H	H	H	H	H
178	NH ₂	H	H	H	H	H
179	N(CH ₃) ₂	H	H	H	H	H
180	N(C ₂ H ₅) ₂	H	H	H	H	H
181	NHCOOCH ₃	H	H	H	H	H
182	NHCH ₃	OCH ₃	H	H	H	H
183	NHC ₂ H ₅	Cl	H	H	H	H
184	NHCH ₂ CH ₂ OH	H	H	H	H	H

Table 5a. Cont.

no	C _{1'}	C ₆	C ₃	C ₅	C _{2'}	C _{3'}
185	N(CH ₂ CH ₂ OH) ₂	H	H	H	H	H
186	N(CH ₃) ₂	Cl	H	H	H	H
187	OH	H	H	H	H	H
188	NHSO ₂ CH ₃	H	H	H	H	OCH ₃

(189-198)

(199)

no	R ₁	R ₂	R ₃	no	R ₁	R ₂	R ₃
189	CF ₃	H	H	190	CF ₂ CF ₃	H	H
191	CF ₂ CF ₂ CF ₃	H	H	192	CF ₂ CHF ₂ CF ₃	H	H
193	CF ₃	CH ₃	H	194	CF ₃	C ₆ H ₅	H
195	CF ₃	CF ₃	H	196	CF ₃	CF ₃	C ₆ H ₅
197	C ₆ F ₅	C ₆ F ₅	C ₆ F ₅	198	CF ₃	COOEt	H

(200-208)

no	R	no	R
200	-CH ₂ CH=CH ₂	201	-CH ₃
202		203
204		205
206	H	207	-CH ₂ CH(CH ₃) ₂
208	-CH ₂ CHO

(209-220)

no	R	no	R
209	CH ₃ CH ₂ CH ₂	210	C ₄ H ₉
211	<i>n</i> -C ₅ H ₁₁	212	<i>i</i> -C ₅ H ₁₁
213	(CH ₃) ₂ NCH ₂ CH ₂	214	HO ₂ CCH ₂
215	HO ₂ C(CH ₂) ₅	216	(CH ₃) ₃ CO ₂ CCH ₂
217	C ₆ H ₅ CH ₂	218	<i>p</i> -ClC ₆ H ₄ CH ₂
219	C ₆ H ₅ (CH ₂) ₂	220	C ₆ H ₅ (CH ₂) ₃

(221)

(222)

(223)

(224)

Table 5a. Cont.

(225)			(226-230)			(231-234)			(235-238)		
no	R		no	R ₁	R ₂	R ₃	no	R			
226	CH ₂ CHO		231	OH	CH ₃	CH ₂ CF ₃	235
227	CH ₂ C(O)CH ₃		232	CH ₃	OH	CH ₂ CF ₃	236
228	CH ₂ CHF ₂		233	OH	CH ₃	C ₂ H ₅	237
229	CH ₂ CF ₂ CH ₃		234	CH ₃	OH	C ₂ H ₅	238
230			(239-258)								
no	Ar	R,R	no	Ar	R,R	no	Ar	R,R			
239	Ph	Me, Me	246	3,4,5-(MeO) ₃ Ph	cycloheptyl	253	4-MeSPh	cyclohexyl			
240	Ph	cyclopentyl	247	4-CF ₃ OPh	cycloheptyl	254	4-MeS(O ₂)Ph	cyclohexyl			
241	Ph	cyclohexyl	248	4-ClPh	cycloheptyl	255	4-NO ₂ Ph	cyclohexyl			
242	Ph	cycloheptyl	249	4-FPh	cycloheptyl	256	4-ClPh	cyclohexyl			
243	4-MeOPh	cyclobutyl	250	4-MeSPh	cycloheptyl	257	4-FPh	cyclohexyl			
244	4-MeOPh	cyclohexyl	251	4-MeS(O ₂)Ph	cycloheptyl	258	4-F ₃ CPh	cyclohexyl			
245	4-MeOPh	cycloheptyl	252	4-EtPh	cycloheptyl
(259-269)			no	Ar	no	Ar	no	Ar			
			259	Ph	260	<i>p</i> -PhPh	261	1-naphtyl			
			262	<i>p</i> -HOCH ₂ Ph	263	<i>p</i> -MeOCH ₂ Ph	264	<i>p</i> -MeOC(O)OCH ₂ Ph			
			265	<i>p</i> -MeC(O)OCH ₂ Ph	266	<i>p</i> -(<i>p</i> '-FPhCH ₂ OCH ₂)Ph	267	<i>p</i> -FPh			
			268	<i>p</i> -F- <i>o</i> -MePh	269	<i>p</i> -CF ₃ Ph
(270-277)			no	R ₁	R ₂	no	R ₁	R ₂			
			270	Cl	CH ₃	271	F	CH ₃			
			272	Br	CH ₃	273	OCH ₃	CH ₃			
			274	Cl	H	275	F	H			
			276	Br	H	277	OCH ₃	H			

Table 5a. Cont.

(278-283)	no	Z	Ar	no	Z	Ar
	278	SO ₂	<i>p</i> -MeOPh	279	SO ₂	<i>p</i> -ClPh
	280	SO ₂	Ph	281	S	<i>p</i> -MeOPh
	282	S	<i>p</i> -ClPh	283	S	Ph

(284-289)	no	R	no	R
	284	—H ₂ C—	285	—H ₂ C—
	286	—H ₂ C—	287	—H ₂ C—
	288	—H ₂ C—	289	—H ₂ C—

(290)	(291)
(292)	(293)
(294)	(295)
(296)
(297)	(298)
(299)	(300)

(301-316)					
no	R ₁	R	no	R ₁	R
301	CH ₃	H	309	CH ₃ (CH ₂) ₂ -	H
302	CH ₃	CH ₃ CH ₂	310	CH ₃ (CH ₂) ₃ -	H
303	CH ₃	CH ₃ (CH ₂) ₂ -	311	(CH ₃) ₂ CHCH ₂ -	H

Table 5a. Cont.

Table 1a. Cont.

no	R ₁	R	no	R ₁	R
304	CH ₃	CH ₃ (CH ₂) ₃ -	312	C ₆ H ₅ (CH ₂) ₄ -	H
305	CH ₃	CH ₃ (CH ₂) ₄ -	313	C ₆ H ₅ (CH ₂) ₂ -	H
306	CH ₃	C ₆ H ₅ (CH ₂) ₃ -	314	<i>p</i> -ClC ₆ H ₄ (CH ₂) ₃ -	H
307	CH ₃	<i>p</i> -ClC ₆ H ₄ (CH ₂) ₃ -	315	(CH ₂) ₂ COEt	H
308	CH ₃ CH ₂	H	316	(CH ₂) ₂ CO ₂ H	H

no	R	no	R
(317-328)	317 CHO 319 CH ₂ OCH ₂ CH=CH ₂ 321 4-CH ₃ C ₆ H ₄ SO ₂ OCH ₂ 323 4-ClC ₆ H ₄ NHCSOCH ₂ 325 CH ₂ OCSNHC ₆ H ₅ 327 4-CF ₃ C ₆ H ₄ CH=CH	318 CH ₂ OCH ₂ CCH 320 4-NO ₂ C ₆ H ₄ COOCH ₂ 322 4-ClC ₆ H ₄ NHCOOCH ₂ 324 4-FC ₆ H ₄ NHCSOCH ₂ 326 4-CF ₃ C ₆ H ₄ CH ₂ NHCO 328 COSC ₆ H ₅

(329)	(330)	(331-347)
--	--	--

no	Aryl nucleophile and site of Attachment	10 Nuc Stereo Chemistry	Product trioxane
331		α	R' = Me
332		α	R' = Allyl
333		α	--
334		α	--
335		α	R' = H
336		α	R' = Me
337		α	R' = Et
338		α	R' = <i>t</i> -butyl
339		α	--
340		α	R' = Me
341		α	R' = PhCH ₂
342		α	R' =
343		α	R' = EtOOCH ₂
344		α	--

Table 5a. Cont.

no	Aryl nucleophile and site of Attachment		10 Nuc Stereo Chemistry	Product trioxane	
345			β	$R'= Cl$	
346			β	$R'= F$	
347			β	$R'= SMe$	
<hr/>
(348-351)	(352)	(353-355)	(356-359)
(360-361)	(362-363)	no	R^4		
		348	Me		
		349	PhCH ₂		
		350	Me ₃ SiCH ₂		
		351	H		
<hr/>					
no	Z	no	Z	no	Z
353	(PhO) ₂ P(O)	354	PhCH ₂	355	<i>p</i> -FPhCH ₂
356	(PhO) ₂ P(O)	357	PhCH ₂	358	<i>p</i> -FPhCH ₂
359	H	360	<i>p</i> -FPhCH ₂	361	H
362	<i>p</i> -FPhCH ₂	363	H		
<hr/>
(364-378)	(373-375)	(376-378)	(379-382)		
no	A	no	R		Z
364	PhCH ₂	373	Ph		O
365	MeOOCPhCH ₂	374	Et		O
366	HOOCPhCH ₂	375	Et		S
367	Et ₂ NC(O)PhCH ₂	no	R	no	R
368	Me ₂ NCH ₂ CH ₂ OOCPhCH ₂	376		377
369	<i>t</i> -BuOOCNHCH ₂	378		no
				382	$R =$
370	Me ₂ N	no	R	no	R
371	Et ₂ N	379	Me	380	PhCH ₂
372	Ph ₂ N	381	CH ₂ :CHCH ₂		

Table 5a. Cont.

<p style="text-align: center;">(383)</p>				
$\text{HO-CH}_2\text{-CH(C}_2\text{H}_5\text{)NH C}_{12}\text{H}_{25}$ (384)		$\begin{array}{c} \text{R}_1 \\ \\ \text{R}_2\text{-N}^+\text{-R}_4 \\ \\ \text{R}_3 \end{array}$ (385-393)		
no	R ₁	R ₂	R ₃	R ₄
385	CH ₃	CH ₃	CH ₃	C ₁₂ H ₂₅
386	C ₂ H ₅	C ₂ H ₅	C ₂ H ₅	C ₁₂ H ₂₅
387	C ₃ H ₇	C ₃ H ₇	C ₃ H ₇	C ₁₂ H ₂₅
388	CH ₃	CH ₃	C ₂ H ₅	C ₁₂ H ₂₅
389	CH ₃	CH ₃	C ₃ H ₇	C ₁₂ H ₂₅
390	CH ₃	CH ₃	C ₄ H ₉	C ₁₂ H ₂₅
391	CH ₃	CH ₃	Br-(CH ₂) ₂	C ₁₂ H ₂₅
392	CH ₃	CH ₃	C ₁₂ H ₂₅	C ₁₂ H ₂₅
393	CH ₃	CH ₃	C ₆ H ₅ -CH ₂	C ₁₈ H ₃₇
394	$\text{C}_{16}\text{H}_{33}\text{-N}^+\text{-(C}_6\text{H}_5\text{)}$			
$\begin{array}{c} \text{R}_1 \\ \\ \text{R}_2\text{-N}^+\text{-CH}_2\text{CH}_2\text{OH} \\ \\ \text{R}_3 \end{array}$ (395-400)	no	R ₁	R ₂	R ₃
	395	CH ₃	CH ₃	C ₁₂ H ₂₅
	396	CH ₃	CH ₃	C ₁₄ H ₂₉
	397	CH ₃	C ₁₂ H ₂₅	C ₁₂ H ₂₅
	398	C ₂ H ₅	C ₂ H ₅	C ₁₂ H ₂₅
	399	C ₂ H ₅	C ₂ H ₅	C ₁₄ H ₂₉
	400	C ₂ H ₅	C ₂ H ₅	C ₁₈ H ₃₇
<div style="display: flex; justify-content: space-around; align-items: flex-end;"> <div style="text-align: center;"> <p>(401)</p> </div> <div style="text-align: center;"> <p>(402)</p> </div> <div style="text-align: center;"> <p>(403)</p> </div> </div>				

Table 5a. Cont.

(404)

(405)

(406)

(407)

(408)

(409)

(410)

(411)

(412)

(413)

(414)

(415)

(416)

(417-431)

no	R ¹	R	no	R ¹	R	no	R ¹	R
417	H	CH ₃	418	CH ₃	H	419	CH ₃ CH ₂	H
420	CH ₃ (CH ₂) ₂	H	421	(CH ₃) ₂ CH	H	422	EtO ₂ CCH ₂	H
423	C ₆ H ₅ CH ₂	H	424	<i>p</i> -ClC ₆ H ₄ (CH ₂) ₂	H	425	C ₆ H ₅ (CH ₂) ₃	H
426	CH ₃	CH ₃ (CH ₂) ₃	427	CH ₃ (CH ₂) ₂	CH ₃ (CH ₂) ₃	428	C ₆ H ₅ CH ₂	CH ₃ (CH ₂) ₃
429	<i>p</i> -ClC ₆ H ₄ (CH ₂) ₂	CH ₃ (CH ₂) ₃	430	C ₆ H ₅ (CH ₂) ₃	CH ₃ (CH ₂) ₃	431	EtO ₂ CCH ₂	CH ₃ (CH ₂) ₃

Table 5a. Cont.

Table S4. Contd.

<p>(432)</p>	<table> <tr> <th>no</th><th>n</th><th>Ar</th></tr> <tr> <td>433</td><td>3</td><td>3,4-(CH₃O)₂C₆H₃</td></tr> <tr> <td>434</td><td>3</td><td>3-CH₃OC₆H₄</td></tr> <tr> <td>435</td><td>4</td><td>3,4-(CH₃O)₂C₆H₃</td></tr> <tr> <td>436</td><td>6</td><td>3,4-(CH₃O)₂C₆H₃</td></tr> </table>	no	n	Ar	433	3	3,4-(CH ₃ O) ₂ C ₆ H ₃	434	3	3-CH ₃ OC ₆ H ₄	435	4	3,4-(CH ₃ O) ₂ C ₆ H ₃	436	6	3,4-(CH ₃ O) ₂ C ₆ H ₃	<p>(433-436)</p>	
no	n	Ar																
433	3	3,4-(CH ₃ O) ₂ C ₆ H ₃																
434	3	3-CH ₃ OC ₆ H ₄																
435	4	3,4-(CH ₃ O) ₂ C ₆ H ₃																
436	6	3,4-(CH ₃ O) ₂ C ₆ H ₃
<p>(437)</p>		<p>(438)</p>		<p>(439)</p>
<p>(440)</p>		<p>(441-448)</p>		<p>(449-451)</p>														
no	R ₁	5-6	R ₂	R ₃ -R ₄	no	R ₁	5-6	R ₂	R ₃ -R ₄									
441	NH		CH ₂	Glu	442	NH		(CH ₂) ₂	Glu									
443	NH	H ₂	(CH ₂) ₂	Glu	444	NH	H ₂	(CH ₂) ₃ Ph-3,4,5-(OMe) ₃										
445	NH		(CH ₂) ₂	Glu	446	NH	H ₂	(CH ₂) ₂ -O-	Glu									
447	O		(CH ₂) ₂	Glu	448	NH	H ₂	(CH ₂) ₂ -S-	Glu									
no	R			no	R			no	R									
449				450	H			451	Ac
<p>(452)</p>					<p>(453)</p>													

Table 5a. Cont.

Table 6. Classification of Inactive Compounds in the Training and Test Set by the Use of LDA-QSAR Models Developed Using Non-stochastic (Eq. 11) and Stochastic (Eq. 12) Quadratic Indices.

name	$\Delta P\%^a$	$\Delta P\%^b$	name	$\Delta P\%^a$	$\Delta P\%^b$
Training Inactive Group					
Amantadine	-97.51	-95.25	Tiazesin hidrokloride	-92.93	-95.47
4- chloro-6-cyano flavan	-98.31	-83.80	Imipraminoxide	-14.81	-42.24
Radicinin	-95.51	-29.28	Prooksen	-98.45	-95.23
TBHQ	-87.02	-88.93	Etoperidone hidrokloride	5.12	51.53
C3-DHCeA	-99.61	-96.38	Befuraline	-97.42	-88.47
BL-1743	-91.34	-81.29	Danitracen	-94.17	-95.52
Dimepranol	-99.82	-99.75	Perithiaden	-97.71	-95.93
LK-274	-99.89	-99.92	Mequitazine	-63.91	-74.70
Riodoxol	-97.44	-93.31	Oxaprotine hidrokloride	-97.39	-95.37
Ethoxene	-99.87	-99.72	Carnidazole	-33.60	-14.30
Ketoxal	-99.31	-99.55	Dimetridazole	-52.78	-76.98
Citenazone	-99.31	-94.88	Hachimycin	-91.90	52.32
Oxolin	-99.79	-92.36	Homidium	89.32	-41.22
Xenygloxal	-99.13	-99.70	Ipronidazole	15.28	17.77
Zalcitabine	-99.00	-93.69	Dimidium bromide	69.23	-80.49
Moroxidine	-99.86	-99.10	N methylglucamine	-99.85	-98.33
Brometenamine	-99.89	-99.79	Oxophenarsine	-63.16	-89.86
Calcii bromoaminoacetat	-99.98	-99.96	Parnaquone	-76.44	0.04
Trichlorourethan	-99.79	-99.95	Antimoniato de meglumina	-99.85	-98.33
Thiourethane	-99.89	-99.51	Nitrofural	1.04	-65.84
Urethane	-99.96	-99.94	Fentanilo	-74.13	-88.88
Etiron	-99.93	-98.95	720 Levacetilmetadol	-24.22	-55.09
Aleudrin"Beckmann"	-99.84	-99.70	721 Metadona	-68.56	-75.31
Chlorobutanol	-97.87	-99.04	724 Oxidodona	-76.67	-40.42
Vernelan	-99.95	-99.89	Morfina	-77.55	-60.77
Sedanfactor Solucion	-99.94	-99.76	Petidina	-95.19	-91.54
Cloretate	-90.67	-99.04	Tilidina	-91.44	-88.16
Alcabrol	-99.36	-99.31	Nalorfina	-65.63	-59.83
Methonal	-99.99	-94.68	Bextrometorfano	-80.69	-87.03
Clomethiazole	-99.57	-97.34	Alylprodine	-68.65	-73.03
Ferriscorbone magnesienne	-99.75	-99.11	Cyclazocine	-40.14	-65.24
Bason	-98.62	-95.38	Desomorphine	-72.85	-69.05
Methylpentynol	-99.33	-98.71	Dezocine	-35.11	-26.46
Carbromide	-98.44	-94.47	Diampromide	-56.89	-68.58
Baldrianol	-99.59	-99.30	Dimenoxadol	-85.57	-81.30
Methenamine	-100.00	-99.98	Dimethylthiambutane	-97.19	-96.98
Paraldehide	-98.94	-99.33	Dipipanone	14.33	10.41
Hedonal	-99.43	-99.42	Hydroxypethidine	-83.79	-76.79
Aponal	-99.21	-99.57	ketobemidone	-79.80	-77.41
Amylurea	-99.70	-99.08	Levallorphan	-45.11	-70.13
Nevanide	-99.10	-99.41	Levorphanol	-73.48	-85.77
Ethchlorvynol	-98.85	-95.40	Meptazinol	-76.96	-83.55
Pentrichloral	-97.98	-99.13	Gobad	-99.79	-99.73
Ectylurea	-99.42	-98.42	Dioxoprometazine	-99.74	-69.09
Almoxatone mesilate	-96.24	-75.18	Phenamicide hidrokloride	-79.81	-70.96

Table 6. Cont.

name	$\Delta P\%^a$	$\Delta P\%^b$	name	$\Delta P\%^a$	$\Delta P\%^b$
Aminogluthetimide	-61.43	-51.66	Difenilhidramine hidrochloride	-98.26	-98.92
Carbavin	-99.84	-99.89	Bromazine	-56.50	-71.39
SOG-18	-96.03	-93.25	Antazoline hydrochloride	-98.72	-97.94
Zonisamide	-93.38	-92.77	Cycliramine maleate	-70.57	-55.10
Acide valproique	-95.60	-93.59	Clorfenoxamine hydrochloride	-89.74	-90.98
LU 2443	-98.75	-99.08	Moxastine hydrochloride	-94.97	-97.58
Chlorphenacemide	-99.77	-99.59	Medrylamine	-96.04	-97.25
Phenacemide	-99.85	-99.84	Metildipenhidramine	-96.35	-97.75
Tetharbital	-97.35	-62.22	Ciclizine hydrochloride	-98.71	-99.21
MECap	-90.51	-87.04	Benzylfenilamino	-97.51	-98.64
UK-17022	-96.12	-3.19	Tolpropamine hydrochloride	-96.64	-98.38
Brofoxine	-94.09	-93.25	Homoclorciclicine	-97.30	-97.00
Norantoin	-99.70	-98.63	Bamipine	-95.08	-97.51
Beclamide	-98.92	-96.83	Pimetixene	-98.20	-94.03
Sultiame	-98.21	-90.45	Etiloxamine hydrochloride	-81.76	-80.17
Albutoin	-91.70	-67.98	Borimamide	-99.28	-92.71
Mephebarbital	-98.50	-95.15	Hiproheptine hydrochloride	-47.02	-19.71
Cinromide	-98.55	-94.09	Nigrifactin	-97.14	-96.67
Zebromal	-96.66	-92.10	Perastine hydrochloride	-88.19	-90.74
Athotoin	-99.11	-94.91	Azatidine maleate	-97.12	-94.87
Fenaclon	-98.41	-94.66	Tironamine	-97.77	-85.88
Pheneturide	-99.23	-98.82	Trazitiline	-64.54	-82.41
Tetrantoin	-98.44	-96.28	Clocinizine	-90.31	-90.24
Metindion	-97.35	-78.91	Quifenadine hydrochloride	-82.03	-90.91
Mesuximide	-99.31	-96.78	Acidum etidronicum	-99.95	-99.93
Metetoin	-98.33	-93.75	Nibet	-99.96	-99.98
Mephenytoin	-97.78	-88.12	Oxiniacic acid	-99.78	-98.90
Primidone	-98.27	-91.89	Acipimox	-98.72	-94.26
Hierro Girard	-99.98	-99.99	Mepiroxol	-99.82	-98.41
Ferroglycine sulfate	-99.99	-99.95	Meglutol	-98.99	-99.43
Ferrosi fumaras	-99.94	-99.95	MTTA	-99.38	-99.57
Fertaron	-99.95	-99.94	Mapyroxal	-99.65	-99.81
Iron aspartate	-99.95	-99.89	Choline glycerophosphate	-100.00	-99.93
Cobalti glutamas	-99.91	-99.78	Acide clofibrique	-96.73	-96.63
Ferrocholate	-99.96	-99.95	Natrii fenbutyras	-99.32	-99.32
Feramid	-99.72	-99.68	Fenbutyramidum	-99.20	-98.87
Ferrosi ascorbas	-99.63	-95.39	Dipiridincarboxan	-93.66	-89.53
Ferrocil	-99.74	-99.93	Penferon	-95.37	-96.89
Fructosum Ferricum	-98.99	-99.53	Acidum sultosilicum	-99.15	-29.99
Ferrotrenine	-99.67	-99.57	Ciprofibrate	-79.74	-87.76
Ferroceron	-96.54	-91.36	Refortan	-95.93	-90.27
Phenolphthalein	-90.71	-51.99	Gemcadiol	6.38	-9.41
Arecoline	-99.73	-99.39	Acetiromate	-77.57	-55.16
Bisacodyl	-61.86	-70.41	Acidum fenofibricum	-92.74	-83.14
Danthron	-93.26	-60.30	Treloxinate	-93.43	-54.27
Emodin	-18.87	28.70	Dulofibrate	-65.36	7.89
Phenolphthalol	-83.73	-89.65	Nicoclonate	-83.79	-26.51
Picosulfate	-99.96	-97.53	Nicofibrate hydrochloride	-68.95	-44.91

Table 6. Cont.

name	$\Delta P\%^a$	$\Delta P\%^b$	name	$\Delta P\%^a$	$\Delta P\%^b$
Butanolum	-99.79	-99.09	Pimetine hydrochloride	-93.90	-98.24
Cupriaseptol	-99.70	-99.36	Itanoxone	-97.57	-92.78
Etamsylate	-96.73	-97.71	Fluperlapine	-90.64	-30.72
Fencadium	-64.82	-93.28	Clorotepine	-93.43	-91.01
Adrenalone	-97.63	-96.73	Azaperone	-61.66	22.58
Carbazochrome sodium sulfonate	-98.83	-98.23	Pecajine	-92.45	-90.67
A-Peest	-93.78	-90.71	Dicarbine	-96.91	-98.16
Ferripyrinum	-96.80	-96.45	Trifluomeprazine	-63.07	-71.51
Hydrastinine hydrochloride	-99.64	-98.55	Meprotixol	-63.42	-77.09
Styptol	-99.14	-95.59	Cianothepin	-97.91	-93.36
Lodal	-99.77	-99.06	Metoxepin	-92.92	-86.25
Morfafen	-84.62	-49.39	Docloxytepin succinate	-85.71	-2.58
Polyurene	-92.72	79.10	Butropipazone	-77.95	-15.34
Pytamine hydrochloride	-42.69	-42.04	Triapride	-96.54	-0.23
DS-511	18.93	23.40	Rolipram	-73.09	-50.74
Hydroxindasate	-79.67	-38.65	Azabuperone	-73.90	-11.01
Cicletanine	-89.45	-66.90	Diclorpromazine	-86.92	-52.44
Metipamid	86.48	98.73	SCH 23390	-95.36	-92.89
Urea	-100.00	-99.99	Timelatem maleate	-89.04	-47.36
Guanamine	-98.23	-97.67	N-hidroxymetil-N-metilurea	-99.97	-99.91
Melamine	-91.53	-92.85	Perhidro,1,2,4,tiadiazine 1,1dioxide	-99.98	-99.71
Glycerol	-99.97	-99.85	5-fluorocitosicine	-99.59	-90.84
Succinic acid	-99.91	-99.96	<i>o,o</i> dietil ditiofosfate	-98.81	-96.65
Pamabron	-99.89	-99.08	Bis(<i>o</i> -etiltiofosfono)disulfide	-80.98	-62.00
Trometamol	-99.97	-99.38	5-bromo-2-metil-5nitro-1,3dioxane	28.38	-67.93
Hydracarbazine	-74.37	-98.81	2,4,5 triclofenol	-98.65	-87.24
Propazolamide	-53.19	-79.34	2,cloro-4nitro fenol	5.54	7.15
Methazolamide	-86.28	-95.88	Clorometil -5-nitro-2-furilketone	-5.07	-1.84
Theophylline-Merodrin	-99.45	-99.64	4- nitrofenol	-31.28	-52.89
Bromothiazide	4.72	-85.89	5-nitro-2-firfurilmetil eter	-30.60	-63.05
Carzenide	-92.29	-99.68	Bis(dimetiltiocarbamoyl)disulfide	-97.34	-99.16
DS-30	-97.02	-97.68	4-bromofenil isotiocianato	-99.79	-98.82
DS-1	-98.57	-99.44	(2-hidroxypropyl trimetilamonium hydroxide	-99.88	-99.86
Oradon	-93.17	-93.48	3,4,5,6 tetrabromo-O-cresol	-94.65	-64.25
Propamin"soviet	-99.94	-99.04	6 cloro-1,2-benzisotiazolidin-3-one	-97.04	-90.24
Cystamine	-99.66	-94.28	6-hidroxi-2-oxobenzoxatiale	-99.62	-97.44
Amifostine	-99.96	-99.57	2,4,6 tribromo-3-metilfenol	-97.40	-85.98
Quimbosan	-98.98	-97.25	4 clorobenzoico acid	-99.79	-99.57
Adeturon	-99.42	-99.83	2 mercapto benzotiazole	-98.80	-98.27
Ficusin	-99.85	-96.33	N(2,2,2 tricloro-1-(4morfolinyl) etil)formamide	-99.00	-99.38
Mexamin	-99.60	-95.91	5(3 Iodopropargyloxy-2-metilio)pirimidine	-96.47	-26.74

Table 6. Cont.

name	$\Delta P\%^a$	$\Delta P\%^b$	name	$\Delta P\%^a$	$\Delta P\%^b$
Peucedanin	-95.40	-13.54	2(4 clorofenoxy)etanol	-99.62	-98.40
Geroquinol	-4.55	-46.79	Fosforotioic acid	-99.18	-95.12
MCHP	-87.11	-97.31	5-etil- <i>p</i> -aminobenzenetiosulfonate	-99.18	-54.97
Meglitinide	-83.13	-70.16	Tricloroetene	-99.78	-99.43
Calcii mesoxalas	-99.95	-99.97	Dimetilsulfoxide	-99.54	-99.84
Metformin	-99.96	-99.68	Trimetilsulfonium hidroxide	-99.93	-99.75
Tiforminhydrochloride	-99.94	-99.48	3-amino-4-hidroxibutanoico acid	-99.96	-99.75
Amformin	-99.23	-87.71	4(2 aminoetil)imidazole	-99.94	-99.21
PIDH	-97.00	-95.04	1H(piridotiazin-one)	-98.63	-98.02
CPSI	-99.97	-81.55	5-sulfonalcyclic acid	-98.80	-99.07
Benfosformin	-99.83	-99.79	2 metoxynitrofenol	14.00	-9.97
Mebenformin	-99.77	-99.09	Salicilic acid dihidrogen fosfate	-99.95	-99.99
Glyclopamide	-62.46	-55.34	1-fenilsemicarbazide	-99.33	-99.87
Carbutamide	-6.12	-2.00	N,N,2-trimetil-1,3-dioxalan-4-ylmetilamine	-99.40	-99.73
Metasulfanilbutylcarbamide	11.57	-1.13	2,2,2 tricloro-4-hidroxiacetanilide	-87.16	-97.76
Anticomman	-94.61	-29.63	4-hidroxiacetanilide	-97.42	-98.31
Furfurylurea	-90.97	-77.67	N-fenil acetidrazine	-96.16	-99.35
Glycyclamide	-52.72	-18.37	8-hidroxi-7-quinoline sulfonic acid	-95.18	-96.25
Tolazamide	5.54	-26.29	<i>o</i> -acetilsalicylamide	-98.73	-98.99
Synthalin B	-77.41	34.10	2-etoxibenzamide	-98.54	-97.95
Scyan	-99.97	-99.93	<i>p</i> -metoxyacetanilide	-97.98	-98.54
Enalaprilat	-69.93	-78.47	Etil- <i>p</i> -amino benzoate	-97.03	-92.16
Ag 307	-99.83	-98.48	4,5,6,7-tetrahidro-2-metil-3-(metilamino)-2H-indazole	-88.92	-92.69
Iodocholine	-99.91	-99.88	Triazino(5,6)quinoline	-92.17	-84.20
Nitricholine perchlorate	-4.92	-96.65	2,3 dihidro-9H-isoxazolo(3,2b)quinazolin-9-one	-96.80	-83.54
Disotat-Amp	-98.49	-95.20	Guanazole	-100.00	-99.94
Guancidine	-92.74	-80.01	Carbetimer	-99.96	-99.58
Diazoxide	-94.38	-84.17	BA 1	-99.98	-99.90
Guanabenz acetate	-98.09	-90.55	Norgamem	-99.95	-99.84
Mebetide	-97.35	-95.66	Cystogon	-99.70	-99.59
Hydralazine	-70.41	-99.02	Mitoguazone	-98.60	-99.52
Tiamenidine	-97.58	-83.44	Pyrimazid	-39.34	-99.26
Alarmin	-98.84	-99.42	Caracemide	-97.56	-98.77
Pildralazine	-39.93	-95.22	Chloromethylsilatrane	-99.98	-99.51
Oxdralazine	-64.75	-96.34	Etimidin	-98.69	-94.59
Clonidine	-96.52	-76.62	Sufosfamide	-99.96	-91.09
MJ 10459-2	-98.92	-93.52	Tegafun	-98.63	-73.50
Olmidine	-99.38	-96.07	Leucenol	-99.76	-97.71
Moxonidine	-67.62	-30.53	Basidalin	-99.66	-96.23
Guanclorfine	-98.74	-78.27	Asperlin	-96.63	-95.39
Oxonazine	50.83	10.09	Pipobroman	-94.70	-70.46

Table 6. Cont.

name	$\Delta P\%$^a	$\Delta P\%$^b	name	$\Delta P\%$^a	$\Delta P\%$^b
Triacetonamine	-82.36	-94.46	Benzotef	-99.78	-97.38
Hemedin	-99.29	-96.40	Glucin	-98.03	-96.89
Guanazodine sulfate	-99.09	-89.33	Dihydroxyacetone	-99.96	-99.92
Penbutamin	-90.33	-96.79	Acesulfame	-99.95	-98.50
Guanisoquine sulfate	-99.63	-98.57	Cyclamic acid	-99.66	-99.32
Tolonidine nitrate	-96.20	-87.04	Melizame	1.21	-73.24
Flutonidine hydrochloride	-94.48	-51.84	Phenetylurea	-98.43	-98.67
Barbismetylii iodidum	-87.17	-41.24	Aspartame	-97.18	-91.34
Vincamine methyl chloride	-35.37	-78.01	S 2346	-98.72	-96.47
Metadiphenii bromidum	-88.40	-87.65	Chinoïn-401	-43.00	36.27
Trimetaphan camsilate	-93.06	-77.85	DL 204 IT	-88.23	-28.35
BAEA	-81.30	-77.15	Clanobulin	-89.48	-69.36
Pentaquinomethonium	-96.52	-91.97	Equilenin	-81.24	-74.34
Phenactropinium chloride	-57.76	-68.25	Diethylstilbestrol	-50.85	-37.63
Pentacynium chloride	-81.28	-88.78	Pipadrol hydrochloride	-79.31	-79.49
Trimethidinium	-82.20	-96.85	Ethyllysergamide	-15.71	-63.27
methosulfate					
Plegarol	-81.02	-89.25	Hexestrol	-22.31	-26.98
Oxamethonium iodide	-83.41	-91.28	Trenbdone	-77.34	-64.11
Oxaditon	-93.91	-97.41	Hydroxyestrone	-38.27	-33.91
Agentit	-96.97	-98.47	Methallenestril	-83.35	-81.08
Dicoline	-39.46	-52.63	Piperazine estrone sulfate	-95.57	-72.42
Fubrogonium iodide	-67.50	-42.05	Sigetin	-77.69	-44.17
Tetramethoquine	-99.36	-97.83	Epiestriol	-40.93	-41.94
methiodide					
Methyloxamethonium	-93.75	-98.34	Nandrolone	-19.31	-27.91
iodide					
Hexamethonium	-98.47	-99.63	Nandrolone sulfate sodium	-85.64	-63.80
Trepirium iodide	-99.27	-99.62	Mecysteine	-99.92	-98.94
Imekhin	-85.17	-97.43	Tuaminoheptane	-98.27	-85.38
Dimecamine	-85.18	-94.61	Tyrosam	-99.68	-98.67
Penhexamine	-82.83	-93.50	Solution A 40	-97.00	-94.61
Mecamylamine	-89.33	-92.05	Methophedrinum	-98.70	-96.16
Leptodactyline	-99.36	-99.64	Proxamine	-98.20	-82.55
Tetrammonii iodidum	-99.97	-99.97	Formetamate	-99.81	-99.42
Methylene chloride	-99.95	-99.78	Indanazoline hydrochloride	-95.02	-92.15
Cryofluorane	-98.36	-99.99	Xylazine	-86.60	-77.96
Frigen 113	-98.07	-99.98	Metizoline	-98.48	-95.48
Teflurane	-99.35	-99.97	Cirazoline	-98.60	-95.49
Norflurane	-99.59	-99.94	Tramazoline hydrochloride	-89.85	-85.34
Tribromethanol	-99.75	-99.79	Phedrazine	-96.04	-88.52
Ethyl bromide	-99.89	-99.34	Naphazoline	-99.53	-98.79
Ethyl chloride	-99.89	-99.29	Tefazoline nitrate	-93.16	11.59
Halopropane	-98.18	-99.09	Domazoline fumarate	-96.57	-90.78
Roflurane	-99.23	-99.86	Xylometazoline	-72.47	-65.27
Methioflurane	-98.40	-98.21	Mtrafazoline	-89.46	-82.61
Cyclopropane	-99.92	-99.78	Racefemine	-81.98	-77.33
Amedalin hidrochloride	-89.56	-60.93	Leiopyrrole	-42.80	-20.07
Noxiptiline hidrochloride	-62.75	-72.85	Nafiverine	36.12	51.58

Table 6. Cont.

name	$\Delta P\%$^a	$\Delta P\%$^b	name	$\Delta P\%$^a	$\Delta P\%$^b
Isopropylum chloratum	-99.67	-98.96	Cypentil	-99.84	-99.22
Sevoflurane	-96.03	-99.74	Zoxazolamine	-99.48	-98.08
Fluroxene	-99.38	-99.93	Emylcamate	-98.28	-98.59
Vinyl ether	-99.89	-99.80	Cresotamide	-97.97	-98.54
Neothyl	-99.75	-99.50	Silamprobamate	-99.73	-90.91
Isopryl	-99.65	-99.65	Meprobamate	-99.16	-99.64
Benzylicum	-99.91	-99.84	Chlorphenesin carbamate	-99.51	-99.05
Metacaine	-96.77	-92.08	Phenprobamate	-99.58	-89.15
Subcutin	-97.03	-92.16	Mephenesin	-99.43	-98.25
Anaesthaminol	-87.41	-76.84	Guaifenesin	-99.38	-97.98
Naretin	-63.35	-63.88	Flucarbril	-99.24	-97.31
Acidum isobutiaticilicum	-92.97	-82.61	Dichlormezanone	-99.84	-64.16
Tireobutil	-24.14	-55.35	Mephenoxalone	-99.35	-97.75
Menthol	-87.81	-81.16	Methocarbamol	-99.46	-99.33
Clormecaine hydrochloride	-90.92	-84.87	Ebubamate	-96.16	-98.20
Butamben	-87.02	-67.76	Strychnocarpine	-88.86	-93.09
Anatiroidol	-99.99	-99.84	Fenyripol hydrochloride	-94.34	-93.44
Basedol	-99.95	-99.77	AHR-2666	-98.42	-93.91
Mercaptothiazoline	-99.95	-99.86	Metaxalone	-98.75	-96.36
Tiouracilo	-98.75	-99.12	Carisoprodol	-85.50	-84.44
Bathyrin	-99.79	-98.91	Pifexole	-88.86	-14.38
Thiamazole	-99.93	-99.89	Quiloflex	-96.48	-90.51
Methylthiouracil	-95.84	-97.89	Clodanolene	-88.14	-19.71
Thiamazol methyl iodide	-99.93	-99.91	Carmecolina cloruro	-99.89	-99.96
Basthioryl	-99.80	-99.82	Furtrethonium iodide	-99.89	-99.86
Propyllthiouracil	-80.82	-88.18	Methacholine chloride	-99.25	-99.77
Carbimazole	-99.61	-97.67	Ezerina	-98.43	-96.67
Bijodtyrosin	-98.02	-94.76	Tetrastigmine	-98.21	-88.35
Fluorotyrosinum	-98.32	-82.34	Pilokarpin	-98.85	-94.36
Thibenzazoline	-99.87	-99.64	Eseridine	-65.82	-78.23
Fenucil	-91.17	-96.70	Distigmine bromide	-77.13	-41.82
Diobutil	-84.66	-35.74	Alifedrine hydrochloride	-10.40	9.24
Thiophenobarbital	-91.77	-66.16	Benzyllephedrine	-96.35	-97.65
Acidum clodronicum	-99.95	-99.98	Isalon Diwag	-70.13	-80.64
Allantovanamide	-99.90	-99.39	Etilefrine pivalate	-67.13	2.50
Orotic	-99.89	-99.61	SY 28	-98.24	-95.52
Imexon	-99.93	-99.50	Pivenfrine	-87.59	-68.98
Isocalcio"Erba"	-99.80	-99.68	Bamethan sulfate	-90.42	-76.17
Treonin fosfatum	-99.98	-99.98	Varon	-98.72	-97.59
Alloxanthine	-63.61	-92.45	Isoprenaline	-79.28	-66.70
Mecytosine	-95.88	-96.73	Detenerol hydrochloride	-93.90	-87.58
Acustasin	-99.93	-99.63	Methoxyphenamine	-98.69	-98.08
Auxinutril	-99.94	-99.52	Mephentermine	-98.32	-98.90
Gaboxadol	-96.10	-92.09	Clorprenaline hydrochloride	-95.87	-82.90
Gluronsan	-99.86	-99.44	Phenylethanolamine	-99.88	-99.38
W 3580 B	-99.61	-99.51	Octopamine	-99.61	-98.20
Didym levulinate	-99.64	-99.82	Norepinephrine	-98.57	-94.65
Pivalylindandione	-95.02	-43.37	Octodrine	-96.34	-79.91

Table 6. Cont.

name	$\Delta P\%$^a	$\Delta P\%$^b	name	$\Delta P\%$^a	$\Delta P\%$^b
Fluindarol	-97.78	-83.66	DIHNE	-95.79	-74.64
Omefin	-99.27	-89.80	Amfetamine	-99.68	-98.70
Xyloucoumarol	-87.82	-60.31	Norephedrine	-99.61	-97.76
Phenprocoumon	-83.49	-41.58	Pulsoton	-98.99	-96.21
Dicumarol	-58.00	55.92	Metaraminol	-98.70	-93.51
Iowarfarin	-53.68	-25.85	Deoxyadrenaline	-98.00	-97.67
Warfarin	-71.56	-56.45	Corbadrine	-95.39	-81.75
Cyclocoumarol	-90.72	-60.55	Isometheptene	-96.69	-96.33
Oxazidione	-97.58	-79.63	Cyclopentamine	-96.65	-95.80
Diphenadione	-96.97	-65.93	Homorennon	-93.14	-82.42
Etiphen	-73.94	24.09	Metamfetamine	-99.44	-99.33
Nitrodimethylin	63.89	-88.03	Ordenina	-99.05	-99.31
Methylis nicotinas	-99.81	-99.30	Etilefrine	-97.85	-93.92
Vasactin	-99.55	-99.61	Methyladrenaline	-95.82	-97.12
Ethiacin	-99.73	-98.70	<i>p</i> -Aminoephedrine	-94.17	-93.99
Nicorandil	80.40	-29.29	Propylhexedrine	-92.96	-92.02
Ampecyclal	-96.44	-86.22	Amezinium metilsulfate	-82.96	-83.47
Carpronium chloride	-99.61	-99.76	1195 L.D.2855	-96.49	-94.02
Sympatektoman-N	-98.00	-96.25	Dichlorisoprenaline	-91.46	-51.99
Nicodan percuton	-98.83	-93.61	Fostedil	-92.85	-60.19
Molsidomine	-42.56	-68.40	Isoxsuprine hydrochloride	-42.97	-19.53
Silidianin	-75.01	6.04	Dilevalol hydrochloride	15.02	-35.36
Sch 24937	-65.89	-24.04	Buphenine hydrochloride	-25.37	-23.85
Axisonitrile	-33.02	-42.78	Papaverine	-80.28	-53.48
Strychnobrasiline	-72.81	-83.50	Chinotoxin	-61.16	-6.31
AY-17605	-98.70	-76.10	Apovincamine	-83.11	-25.74
Cloguanamil	-99.30	-90.26	Vincamine	-40.90	-16.44
Dabhekhin	-36.27	-45.54	Ifenprodil tartrate	-20.06	-58.82
Feclomine	-41.27	-60.07	Diprofenehydrochloride	-12.91	12.90
Etomiololine	-46.70	-60.53	Nicergoline	-48.64	9.19
Hexalorxylol	-93.86	-95.27	Prenylamine	-76.07	-84.53
Supazine	29.66	-88.95	Ericolol	-25.22	46.62
Antimony sodium tioglycollate	-98.77	-99.75	K 4423	-60.69	-12.16
Dichorus	-99.82	-99.64	Penbutolol sulfate	-7.78	5.15
Metriponate	-99.36	-98.81	Pafenolol	-25.25	49.27
Safersan	-99.77	-99.42	Tolamolol hydrochloride	-70.13	-54.53
Lindane	-88.84	-30.44	IPS 339	-0.27	35.97
Actractil	-94.32	-80.28	Bevantolol hydrochloride	-67.12	-36.11
Bitricanate	-99.79	-98.20	Butyroxane	-67.06	-42.62
Certuna	-92.98	-97.76	Butopamine	-26.56	-26.28
Metilarecaidine	-99.73	-99.39	Dobutamine hydrochloride	23.92	10.89
Punicine	-97.96	-96.69	Carbazeran	36.61	69.35
Antienite	-99.75	-98.76	Neo-Coronaril	-64.60	-68.98
Bromotimol	-92.25	-83.00	Phenothrin	-11.69	12.96
Iodotimol	-92.89	-87.77	Bromopropylate	-39.63	-6.56
Famopos	-99.95	-86.92	Proclonol	-82.02	-57.95
Eucaliptol	-82.10	-94.51	Tibenzate	-99.33	-98.09

Table 6. Cont.

name	$\Delta P\%^a$	$\Delta P\%^b$	name	$\Delta P\%^a$	$\Delta P\%^b$
Antafenite	-99.80	-99.20	Iodofenphos	-96.90	-67.06
Nitramisole hydrochloride	-22.50	-2.81	Asame	-98.93	-99.04
Pyrantel tartrate	-99.37	-98.43	EN-3638	-25.53	-49.23
Vincofos	-59.47	-43.54	KC-8973	-88.05	34.49
Feniodium chloride	-93.09	-24.05	Ethydine	-71.66	23.10
Phoxim	-58.89	29.59	Orazamide	-99.45	-98.55
Antiolimine	3.39	-99.14	Xanthine	-99.13	-97.15
Cetovex	-87.32	-60.10	Tiopronin	-99.76	-99.45
Crufomate	-96.65	-88.21	Nicoxamat	-98.11	-99.92
Pexantel	-94.02	-92.46	Acidum metioformicum	-99.32	-98.67
Ciclopramine	-92.32	-92.79	Orotosan S	-99.43	-97.57
Dibenzepine Hydrochloride	-98.48	-94.11	Magnesii metioglicas	-99.13	-99.93
Mezepine	-98.27	-97.60	Ethyl glutamate	-99.38	-96.94
Bifemelane Hydrochloride	-97.98	-91.30	Succinyl-Methionine	-97.41	-97.57
Tandamine Hydrochloride	-90.82	-84.00	Acidum methenoxycinnamicum	-99.80	-99.47
Demexiptiline hydrochloride	-91.30	-83.12	Alibendol	-86.89	-77.36
Cimoxatone	-93.78	-89.29	Aminopromazine	-94.55	-97.23
Perafensine	-99.29	-94.14	Butaverine	-38.55	-37.16
Fluperlapine	-96.93	-55.98	N-Butylscopolammonium Bromide	-44.07	-34.80
Elanzepine	-96.13	-90.24	Cimetropium Bromide	-89.78	-90.74
Nortriptyline	-98.44	-97.45	Cinnamedrine	-93.50	-96.45
Mariptiline hydrochloride	-91.35	-59.06	Emepronium Bromide	-91.67	-97.02
Pridefine hydrochloride	-97.92	-96.89	Fenpiverinium Bromide	-71.41	-93.01
Doxepin hydrochloride	-98.28	-96.76	Flopropione	-74.85	-59.25
Dosulepin hydrochloride	-97.99	-97.53	Hymecromone	-99.14	-94.88
Test Inactive Group					
DCF, BW 683c	-94.69	-78.48	Bis(etilmercuri)sulfide	-81.90	-73.38
3-Episiostatin B	-99.42	-98.41	Pentaclorofenol	-94.01	-9.38
Thiacetazone	-85.50	-91.77	Cloro(2 hidroxifenil)mercurio	-96.99	-99.23
Foscarnet	-99.99	-99.99	<i>o,o</i> dimetil-1-acetoxy 2,2,2 triclорometanefosfonate	-96.46	-98.26
IMPY	-99.54	-99.10	3,5 dibromosalicylaldehyde	-99.31	-95.32
SKF-23880 A	-98.35	-89.39	3,5 dibromosalicylcy amide	-96.91	-94.78
Cloral betaine	-99.85	-99.98	1-hidroxi-4,6-dimetil pirididone	-94.83	-98.45
Isopral	-99.29	-99.44	5(3 cloropropyl)4-metiltiazole	-99.07	-94.89
Bromobutanol	-97.76	-98.89	3 acetil-6-metil-2H-pyran-2,4(3H)dione	-98.71	-94.34
Agr 449	-99.90	-99.85	5-fenil-3-(triclорometil)tio 1,3,4-oxadioxol 2 (3H)one	-57.11	-84.64
Valerium Paul Thibault	-99.57	-99.48	1-Pirazolecarboxamidine	-99.76	-99.55
Cetohexazine	-97.01	-97.78	Carbamimidotioic acid	-99.83	-98.48
Ciproximide	-98.47	-92.69	Fenoverine	-95.61	-44.62
Metiapine	-94.13	-92.02	Flavoxate	-54.32	78.41
Cintramide	-97.47	-96.25	Hydramitrazine	65.98	13.60
Tetrabenazine mecilate	-29.42	-11.80	Moxaverine	-77.66	-52.13

Table 6. Cont.

name	$\Delta P\%^a$	$\Delta P\%^b$	name	$\Delta P\%^a$	$\Delta P\%^b$
Bromisoval	-99.39	-98.64	Pirocatecol-3,5 disulfonic acid	-74.70	-94.23
Calcii diethylacetat	-99.05	-98.29	tiosalicilic acid	-99.46	-99.70
Gallochromolum	-79.73	-74.91	2 hidroksibenzamin	-99.25	-99.37
Mepentamat	-99.65	-99.63	5-amino-1-fenil-1H tetrazol	-35.42	-85.75
Trimetadion	-99.65	-98.45	propil-5-tiazol karboksilic acid	-99.03	-97.91
Valpromid	-96.24	-89.56	Acetanilid	-99.18	-99.42
Atrolaktamid	-99.27	-99.24	3-hidroksiacetanilid	-97.35	-98.30
IL-16	-98.01	-96.43	<i>o</i> -acetil-5-bromosalicilic acid	-98.77	-98.20
Buramat	-99.73	-99.51	<i>o</i> -acetil-3-iodosalicilic acid	-98.87	-98.71
Phensuximid	-99.67	-98.66	<i>o</i> -Karbamoilpenoksilic acid	-99.29	-99.76
Nirvanol	-96.91	-92.68	N-metil acetanilid	-99.66	-99.61
Phenobarbital	-96.63	-87.52	4-hidroksipropionalilid	-94.25	-92.10
Phenitilone	-96.73	-92.02	<i>p</i> -Etoksilanilometan sulfonic acid	-99.32	-97.11
Tiletamin hidroklorid	-86.27	-56.42	2-isopropil-4-pentenil urea	-98.10	-97.47
Ferro-Drops	-99.94	-99.90	7 Kloro-3,3 dihidro-2H,9H isoksazol benzoksazin	-89.57	-46.07
Orotansan Fe	-99.74	-99.41	6,7dihidroksi-4-metil kumarin bis (hidrogen sulfat)	-99.99	-96.80
Kobalt besilas	-99.93	-99.78	Hadacidin	-99.77	-99.97
Sodium dipantoylferrat	-99.64	-99.43	Fluoksipilin	-99.24	-94.49
Aloe-Emodin	-75.22	29.25	Propanoic acid	-99.91	-99.87
Oksifenisatin Acetat	-75.54	-24.82	Fluorembihin	-99.44	-96.30
Bibrofenum	-98.88	-93.82	Etretin	-42.65	-62.90
Sango-Stop	-99.74	-99.00	Tetramin	-99.87	-99.72
Naftazon	-98.64	-98.86	Mitobronitol	-99.41	-92.61
Iprazokrom	-71.10	-86.45	Imifos	-99.45	-92.40
Lemidosul	-91.91	-44.66	Spiroplatin	-99.57	-93.52
Glykuril	-99.98	-99.98	Azapikil	-95.02	-98.53
Acetazolamid	-76.25	-95.35	Uramustine	-96.77	-77.51
Oksaden	-75.55	-88.66	Novembitol	-99.05	-97.06
Kloromerodrin	-98.47	-99.61	Nifuron	96.33	93.92
Manna sugar	-99.89	-98.53	Razoksan	-94.00	-92.87
Sulklamid	-57.01	-97.69	Xiloz	-99.93	-99.68
Mateina	-99.95	-97.67	Benzosulfimid	-98.69	-96.81
Pallirad	-99.98	-99.18	Dienestrol	-77.09	-75.40
WR 2823	-99.82	-98.39	Vinkonat	-95.37	-74.79
Beroksan	-99.65	-89.53	Equilin	-65.86	-66.91
TA-078	-65.72	-51.24	Estrone	-35.04	-45.92
Tonyol	-99.95	-99.94	Drupanol	-32.62	-74.81
Etoformin hidroklorid	-98.12	-75.79	Estradiol	-33.34	-47.22
Phenformin hidroklorid	-99.73	-97.95	ASL-7003	-97.18	-93.71
Phenbutamid	-90.96	-68.94	Amidefrini mesilas	-98.95	-97.90
Centpiperalone	-98.48	-92.33	Mefentermin	-98.32	-98.90
Klomoksil sodium	-86.48	-88.61	Tetrazolin hidroklorid	-98.50	-96.42
Gliparamid	-49.24	-50.13	Fenoksazolin	-96.56	-88.36
Urefibrat	-95.89	-78.84	Karoverin	-58.45	10.45
Klofenapik acid	-92.30	-91.87	Diisopromin	-29.24	-71.82

Table 6. Cont.

name	$\Delta P\%$^a	$\Delta P\%$^b	name	$\Delta P\%$^a	$\Delta P\%$^b
Bromcholine	-99.91	-99.86	Clonazoline hydrochloride	-99.00	-94.97
Abbott-31699	76.50	-33.99	Coumazoline	-96.75	-88.67
Guanoxabenz	-81.66	-97.83	Tymazoline hydrochloride	-92.83	-77.07
Dihydralazine	76.32	-99.21	Isopropylmethoxamine	-69.28	-32.03
MK-534	-98.50	-96.89	Oxymetazoline hydrochloride	-4.93	-10.79
Guanfacine hydrochloride	-99.08	-90.01	Orphenadrine hydrochloride	-96.35	-97.61
Guanoclor sulfate	-98.26	-86.10	Chlorzoxazone	-99.36	-97.11
Guanacine sulfate	-99.71	-98.74	Dimebamate	-99.82	-99.93
Guanoctine hydrochloride	-92.72	-87.38	DEP	-98.89	-95.20
Nicopholine	-99.40	-98.01	Styramate	-99.87	-99.89
Stilonium iodide	-72.25	-71.00	Betaquil	-99.68	-99.82
Paramyon	-75.15	-88.80	Glyketal	-82.39	-88.09
Gaplegin	-87.98	-95.64	Promoxolane	-82.48	-72.63
Dimecolonium iodide	-95.61	-98.46	Chlormezanone	-99.92	-88.75
Chlorisondamine chloride	-97.57	-84.76	Mephenesin carbamate	-99.50	-99.42
Tiamethonium iodide	-97.11	-98.31	Murexine	-99.44	-99.06
Temechin	-78.20	-95.11	Tartrate	65.98	13.60
Cyclocholine tosilate	-99.97	-99.94	Nafomine	-98.02	-99.73
Halothane	-99.39	-99.97	Luvatren	-97.45	-91.76
Ethylene	-99.96	-99.88	Lorbamate	-93.03	-91.79
Methoxyflurane	-99.27	-99.89	Fenylamidol hydrochloride	-95.71	-95.72
Aliflurane	-94.66	-93.53	Tybamate	-77.74	-70.54
Vinamar	-99.80	-99.60	Acetylcholine	-99.75	-99.90
Saligenol	-99.72	-99.46	Dithiophos	-69.65	14.35
Novasil	-97.49	-95.04	Pyrophos	-92.26	-55.37
Risocaine	-93.73	-82.04	Pyridostigmine bromide	-99.88	-99.63
Isobutamben	-87.08	-73.42	TV 399	-51.09	-70.60
Iodothiouracil	-97.71	-98.27	Doxaminol	-70.89	-64.08
Aminomethiazole bitartrate	-99.84	-99.52	MK-801	-89.08	-96.08
Mipimazole	-99.24	-97.79	Methyphemin,M6T	-95.73	-97.06
Beta-Dijodtyrosin	-95.72	-94.63	Etafedrine hydrochloride	-96.86	-96.82
Bentiuracil	-87.56	-96.12	Dimetofrine hydrochloride	-95.18	-92.61
Dimaval	-99.96	-99.51	Orciprenaline sulfate	-79.18	-66.72
Quisqua lamine	-99.68	-98.20	Isofenefrine	-93.73	-87.49
Pyrglutargine	-99.85	-99.67	Alfetamine	-99.30	-98.17
Eutrit	-99.93	-99.31	Dioxethedrin	-78.13	-54.45
Esorben	-99.83	-98.92	Norfefrine	-99.60	-98.18
Anisindione	-99.23	-90.24	Dopamine	-98.88	-96.04
N. H. C	-95.55	-80.77	Oxidopamine	-95.55	-87.26
Napharin	-47.36	7.68	Pacamine	-96.22	-92.10
Dan Shen-Su	-97.50	-98.43	Adrenaline borate	-92.83	-99.08
577 Cycloleucine	-99.68	-98.48	Cathine	-99.61	-97.76
Percloroetane	-97.39	-99.89	Hydroxyamfetamine	-99.01	-96.23
Dimetrizadole	-54.09	-70.09	Phenylephrine	-99.27	-98.91
Fospirate	-98.37	-83.15	Synephrine	-99.29	-98.92
Butonate	-96.87	-91.66	Ephinephrine	-97.44	-96.78
lobendazole	-89.45	-92.84	Phenamazoline	-99.11	-98.18
Clofibrate	-82.10	-59.78	Apoatropine	-91.37	-90.15

Table 6. Cont.

name	$\Delta P\%$ ^a	$\Delta P\%$ ^b	name	$\Delta P\%$ ^a	$\Delta P\%$ ^b
Antazonite	-97.91	-92.73	Pholedrine sulfate	-98.28	-98.03
Tioxidazole	-92.94	-74.97	Oxyephedrine	-97.81	-96.56
Morantel tartrate	-98.67	-96.56	Dioxifedrine	-92.10	-89.97
Amendol	-81.69	-37.66	Metanephrene	-98.15	-97.16
Desipramine dibudinate	-97.48	-94.83	AMT	-91.48	-90.95
Adinazolam	-89.35	-56.93	Phenoxybenzamine	-86.38	-85.01
Protriptyline hydrochloride	-98.21	-98.38	Benfurodil hemisuccinate	-82.14	-25.10
Spiroxeptin	-96.11	-89.62	Aligeron	-96.83	-98.20
Ketimipramine	-95.97	-92.18	Belarizine	-87.80	-93.91
Binedaline hydrochloride	-91.65	-98.51	Odiphalin	-58.60	-57.25
Cotriptyline	-97.97	-97.56	Iprocrololhydrochloride	34.44	95.20
Litracen	-97.78	-92.14	PHQA 33	-80.04	-21.47
Furazolidone	80.62	38.98	Exaprolol hydrochloride	-23.94	20.35
Clioquinol	-90.38	-76.41	Betaxolol	-35.66	-5.06
Hidrocodona	-78.12	-47.96	Bornaprolol hydrochloride	-31.24	-5.49
723 Noscapina	-96.98	-38.51	Chinoïn 103	-66.74	-11.81
Amiphenazole	-94.84	-97.02	D 2343-HCl	14.08	-3.73
Codeinemethylbromide	-95.31	-90.33	ROM-203	-88.47	-48.98
Dextromoramide	-42.81	-33.84	Flusoxolol	44.21	92.27
Dimepheptanol	-54.81	-76.41	Canfochinid	-56.15	-61.41
Tenalidine tartrate	-88.41	-86.32	Tioctilate	-55.25	-2.99
Fenyltoloxamine	-97.61	-98.37	Thanite	-76.10	-64.71
Prometazine hydrochloride	-95.85	-95.63	Heptenophos	-99.60	-98.43
meflophenhidramine	-86.79	-66.12	Arphamenine A	-95.45	-71.40
Ametobenzepine	-96.89	-97.35	Lipothiamine pyrophosphate	-95.00	-99.40
Histamithizine	-82.79	-84.28	Homocysteine thiolactone	-99.90	-98.15
Tripolidine hydrochloride	-77.51	-83.74	Tioliacic	-99.90	-99.85
Histapipendine	-89.69	-93.64	Oxomethionine sodium	-99.75	-99.52
Colestipol	-99.99	-99.03	Citolone	-99.32	-97.58
Nicomethanol	-99.86	-99.71	Methioninol	-99.83	-99.67
Acide tizoprolique	-98.75	-98.33	Thioctamide	-82.66	-88.67
Metexaminum	-98.25	-87.20	Ambucetamide	-20.18	-20.06

^aResults of the classification of compounds obtained from Eq. 11 (using non-stochastic quadratic indices);

^bResults of the classification of compounds obtained from Eq. 12 (using stochastic quadratic indices): $\Delta P\% = [P(\text{Active}) - P(\text{Inactive})] \times 100$; where P(active) is the probability that the equations classify a compound as active. Conversely, P(Inactive) is the probability that the models classify a compound as inactive. This value ($\Delta P\%$) takes positive values when $P(\text{active}) > P(\text{Inactive})$ and negative otherwise. Therefore, when $\Delta P\%$ is positive (negative) the compound was classified as antimalarial (non-antimalarial).

Chemistry and Data Analysis

IR spectra were recorded with a FTIR-BOMEM spectrometer using KBr disks for solid or NaCl cell for liquids (ν in cm^{-1}). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker ADPX-300 (300 MHz) using CDCl_3 as solvent. The calibration of spectra was carried out on TMS (internal ^1H) and CDCl_3 (^{13}C) signals δ ^1H (TMS) = 0; δ ^{13}C (CDCl_3) = 77.0. Chloroquine diphosphate was supplied by “Fundação para o Remédio Popular” (Brazil). All solvent were previously dried and purified before use, according to standards established in the literature.

(Z)-ethyl 3-(phenylamino)but-2-enoate (1)

Neutral aluminum oxide (40 g) was added to a stirred mixture of ethyl acetoacetate (100 mmol) and aniline derivative (100 mmol), and stirring was continued for 24 h (controlled by GC) at 80°C . The reaction mixture was washed and filtered with CHCl_3 , and the filtrate was evaporated. The crude product was separated by fractional distillation at reduced pressure. Yield: 15.98 g (77.9 %); yellow liquid; b.p. 110°C (0.1 mm Hg).

^1H NMR (CDCl_3) δ (ppm): 1.24 (t, 3H, $J=7.1$ Hz, H-2'), 1.99 (s, 3H, H-4), 4.17 (q, 2H, $J=7.1$ Hz, H-1'), 4.69 (s, 1H, H-2), 7.08 (d, 2H, $J=7.5$ Hz, $o\text{-H}_{\text{arom}}$), 7.15 (t, 1H, $J=7.5$ Hz, $p\text{-H}_{\text{arom}}$), 7.32 (t, 2H, $J=7.5$ Hz, $m\text{-H}_{\text{arom}}$), 10.38 (s, 1H, NH); ^{13}C NMR (CDCl_3) δ (ppm): 14.74, 20.46, 58.9, 86.18, 124.55, 125.06, 129.19, 139.49, 159.09, 170.55.

Diethyl (anilinomethylene)malonate (2)

Stirred mixture of aromatic aniline (20 mmol) and ethyl orthoformate (10 mmol) was warmed for 2 h at $135\text{--}130^\circ\text{C}$. Later, orthoformate (10 mmol), ethyl malonate (10 mmol)

and 0.2 g of zinc chloride catalyst were added. The mixture was stirred and refluxed for 5 hours. Soon after ethyl malonate (10 mmol) was added. The reaction was kept in these conditions for 15 hours (controlled by GC). The reaction mixture was extracted with ether. The combined organic layers were washed with water and dried over MgSO₄. The solvent was evaporated under reduced pressure and the crude product was separated from the unreacted starting material by fractional distillation at reduced pressure. Yield: 4.67 g (88.62 %); b.p. 101 °C (0.35 mmHg); colorless liquid.

IR: 3548 (N-H); 3054 (C=C); 1693 (C=O); 1650 (C=C); 850, 690, 614 cm⁻¹ (C-H). ¹H NMR (CDCl₃) δ (ppm): 1.33 (t, 3H, *J*=7.4 Hz, CH₃), 1.38 (t, 3H, *J*=7.4 Hz, CH₃), 4.25 (q, 2H, *J*=7.4 Hz, CH₂), 4.31 (q, 2H, *J*=7.4 Hz, CH₂), 7.17 (d, 2H, *J*=7.5 Hz, *o*-H_{arom}), 7.18 (t, 2H, *J*=7.5 Hz, *m*-H_{arom}), 7.37 (t, 1H, *J*=7.5 Hz, *p*-H_{arom}), 8.54 (d, 1H, *J*=13.5 Hz, CH), 11.0 (d, 1H, *J*=13.5 Hz, NH); ¹³C NMR (CDCl₃) δ (ppm): 14.49, 14.61, 60.34, 60.61, 93.64, 117.37, 125.13, 130.01, 139.41, 152.14, 165.97, 169.25.

Ethyl 3-(3-ethoxy-2-(ethoxycarbonyl)-3-oxoprop-1-enylamino)benzoate (3)

This compound was prepared in an analogous form to 2.

Yield: 3.79g (56.45%); m. p. 52-53 °C; beige solid.

IR: 2983, 893, 792, 755 (C-H); 1692, 1641 (C=O); 1591, 1424 (C=C); 1260 (C-O-C); 1096 (C-O).

¹H NMR (CDCl₃) δ (ppm): 1.35 (t, 3H, *J*=7.1 Hz, CH₃), 1.37 (t, 3H, *J*=7.1 Hz, CH₃), 1.39 (t, 3H, *J*=7.1 Hz, CH₃), 4.16-4.36 (m, 6H, 3 x CH₂), 7.36 (d, 1H, *J*=7.7 Hz, H_{arom}), 7.45 (t, 1H, *J*=7.7 Hz, *m*-H_{arom}), 7.89 (d, 1H, *J*=7.7 Hz, H_{arom}), 7.95 (s, 1H, *o*-H_{arom}), 8.58

(d, 1H, $J=13.5$ Hz, CH), 11.1 (d, 1H, $J=13.5$ Hz, NH); ^{13}C NMR (CDCl_3) δ (ppm): 14.01, 60.56, 93.96, 117.83, 121.06, 126.3, 129.7, 131.8, 139.3, 151.6, 166.0, 168.7, 170.1.