CHAPTER IV

FITTING OF ELECTRON DISTRIBUTION TO THE ACTIVITY OF DRUGS BY LINEAR MODELS

After evaluation of atomic populations, numerous possible multi-linear relationships between these data and the pharmacological activity were statistically tested. The same procedures have been done for both CNDO/2 and Ab-initio framework. The object was a model containing as few parameters and variables as possible, but still describing the drugs' activity correctly within the limits set by physiological variation of pharmaceutical data. The general equation for such relation is chosen as:

$$\ln A = \sum_i p(i)*q(i) + pu*u + D \qquad (4.1)$$

where A = the relative activity in percent of the drugs

$p(i)$ = the fitted parameter for the i th atom

and $q(i)$ = the net charges of that atom

$= \rho_i - Z_i$

ρ_i = calculated electron density of atom i

Z_i = valence electron of atom i

u = dipole moment of molecule

D = the additional fitting parameter

For all models, parameters have been fitted by linear regression program (APPENDIX III), assumming Gaussian distribution.

The model of equation 4.1 has also been extended as following:

$$\ln A = \sum_i p(i)*q(i) + p(u)*u + p(rest)*q(rest) + D \qquad (4.2)$$

where q(i) = atomic net charges of interested atoms in quinoline ring

q(rest) = summation of net charge in quinoline ring after exclusion of q(i)

4.1 Fitting of the Linear Equations of Chloroquine by CNDO/2 Method

The calculated net charges of chloroquine compounds that have been used in linear model fitting are listed in table 4.1.

Searching for the suitable linear models of the type described in equations 4.1 and 4.2, the relative importance of atoms in the molecule can be gradually recognized from the parameter size. This allows exclusion of less important atoms for the sake of a more simple model and to evaluate gradually the structure of the active center of the drug.

Fitting of the linear equations for various steps of atom inclusion led to the parameters listed in tables 4.2a - 4.2c. According to the large value of some parameters obtained from model 0 in table 4.2a, the more interesting atoms are:

N1, C2, C3, C4, C9, C10 and N2.

Therefore, C5, C6, C7, C8 which have small parameters are grouped together as qC(5-8) and sometimes referred to as qrest in various models.

The quality of the model was indicated by the standard deviation of predicted and observed activity, SD , given in the

same table. The definition of various parameters are:

p = parameters for net charges, q(i), of atoms

prest = parameters for qrest

pu = parameters for calculated dipole moment (debyes)

SD = the standard deviation between calculated and observed ln A

$$= \sqrt{\frac{[(\ \ln A) - (\ \ln A)]^2}{N-1}}$$

Cmax = maximum deviation observed throughout the series

D = parameter corresponding to equation 2.

Table 4.1 The net charges for CNDO/2 calculation of atoms in chloroquine drugs as use for linear model fitting

Compound	Net Charges of Atoms										
no.	N1	C2	C3	C4	C5	C6	C7	C8	C9	C10	N2
CQ1	0.1953	-0.1275	0.1075	-0.1598	-0.0195	0.0160	0.1180	0.0340	-0.1180	0.0121	0.2286
CQ2	0.2014	-0.1313	0.1141	-0.1648	-0.0376	0.0784	0.2561	0.1011	-0.1345	0.0283	0.2291
CQ3	0.1943	-0.1284	0.1066	-0.1594	-0.0193	0.0066	0.0171	0.0232	-0.1183	0.0093	0.2285
CQ4	0.2044	-0.1310	0.1166	-0.1651	-0.0359	0.0868	-0.2059	0.0978	-0.1333	0.0314	0.2295
CQ5	0.2015	-0.1267	0.1128	-0.1603	-0.0205	0.0346	0.0670	0.0590	-0.1195	0.0208	0.2295
CQ6	0.1983	-0.1243	0.1097	-0.1577	-0.0158	0.0195	-0.0357	0.0413	-0.1164	0.0149	0.2295
CQ7	0.1978	-0.1299	0.1100	-0.1628	-0.0288	0.0584	-0.0423	0.0421	-0.1234	0.0170	0.2287
CQ8	0.1863	-0.1287	0.1092	-0.1614	-0.0259	0.0226	-0.0438	-0.0374	-0.1272	0.0160	0.2284
CQ9	0.1970	-0.1275	0.1103	-0.1648	-0.0952	0.0073	-0.0327	0.0325	-0.1175	0.0087	0.2352
CQ10	0.1896	-0.1223	0.1042	-0.1535	0.0043	0.0275	-0.1010	0.0248	-0.1100	0.0074	0.2291
CQ11	0.1794	-0.1101	0.0363	-0.1347	-0.0224	0.0235	-0.1190	0.0364	-0.1127	0.0127	0.2430
CQ12	0.2196	-0.1595	0.1216	-0.1635	-0.0221	0.0206	-0.1206	0.0387	-0.1217	0.0180	0.2289
CQ13	0.1841	-0.1184	0.1009	-0.1522	0.0096	-0.0032	-0.0711	-0.0921	-0.0827	-0.0016	0.2288
CQ14	0.1885	-0.1251	0.0810	-0.1449	-0.0602	0.0618	-0.1367	0.0669	-0.1276	0.0412	0.2159
CQ15	0.1884	-0.1256	0.0810	-0.1451	-0.0604	0.0617	-0.1370	0.0671	-0.1279	0.0410	0.2157
CQ16	0.1885	-0.1249	0.0810	-0.1447	-0.0602	0.0618	-0.1368	0.0672	-0.1276	-0.1276	0.0414
CQ17	0.1882	-0.1249	0.0809	-0.1446	-0.0610	0.0620	-0.1370	0.0671	-0.1273	0.0411	0.2157
CQ18	0.1947	-0.1272	0.1076	-0.1593	-0.0191	0.0161	-0.1178	0.0338	-0.1189	0.0125	0.2288
CQ19	0.2026	-0.1280	0.1078	-0.1653	-0.0234	0.0167	-0.1168	0.0376	-0.1170	0.0084	0.2269
CQ20	0.1970	-0.1310	0.1919	-0.1608	-0.0204	0.0173	-0.1188	0.0350	-0.1206	0.0138	0.2223
CQ21	0.1962	-0.1310	0.1915	-0.1607	-0.0205	0.0169	-0.1188	0.0347	-0.1206	0.0138	0.2221
CQ22	0.1965	-0.1314	0.0906	-0.1608	-0.0205	0.0166	-0.1191	0.0345	-0.1208	0.0135	0.2219

Table 4.2a Parameters for linear model and fitting characteristics of the equation including all CNDO/2 net charges of all atoms in quinoline ring and N2 of chloroquine drugs (no. of compounds = 22)

Model	Parameters												SD	C max
	pN1	pC2	pC3	pC4	pC5	pC6	pC7	pC8	pC9	pC10	pN2	D		
0	327.758	174.463	-48.297	406.392	7.354	35.947	2.371	-18.329	-236.367	-227.709	48.234	10.631	0.837	1.793

Table 4.2b Parameters for linear model and fitting characteristics of the equation including CNDO/2 net charges of atoms N1, C2, C3, C4 and N2 of chloroquine drugs (no. of compounds = 22)

Model	Parameters									SD	C max
	pN1	pC2	pC3	pC4	pC(9,10)	pN2	pC(5-8)	pu	D		
1	67.741	50.690	22.132	95.115	-	-	-	-	9.168	1.149	1.716
2	112.584	83.682	-14.734	91.254	-	15.511	-	-	4.351	1.081	1.722
3	214.129	116.288	-31.214	311.266	-155.594	18.056	-7.867	-	7.440	1.045	1.685
4	162.964	133.555	10.609	160.340	-	16.733	-	0.381	6.596	0.962	1.483
5	216.743	119.062	-29.616	314.079	-155.335	37.365	2.922	0.021	4.280	0.941	1.835

Table 4.2c Parameters for linear model and fitting characteristics of the equation including CNDO/2 net charges of atoms N1, C4, C9, C10 and N2 of chloroquine drugs (no. of compounds = 22)

Model	Parameters									SD	C max
	pN1	pC(2,3)	pC4	pC9	pC10	pN2	pC(5,8)	pu	D		
6	25.301	-	60.471	-61.050	-10.825	-	-	-	0.493	1.145	1.726
7	-18.174	-	127.214	-149.452	-94.195	15.815	-	-	7.201	0.889	1.221
8	66.748	4.180	235.322	-122.113	-98.533	18.960	2.864	-	10.171	1.028	1.102
9	-10.102	-	154.477	-168.838	-121.611	17.356	-	-0.294	9.515	0.846	1.098
10	67.608	5.675	236.678	-122.063	-97.902	18.756	2.834	0.014	10.211	1.028	1.706

Table 4.2d Parameters for linear model and fitting characteristics of the equation including CNDO/2 net charges of atoms N1, C2, C3, C4, C9, C10 and N2 of chloroquine drugs (no. of compounds = 22)

Model	Parameters										SD	C max
	pN1	pC2	pC3	pC4	pC9	pC10	pN2	pC(5,8)	pu	D		
11	-89.267	-27.760	35.729	78.985	-132.059	-59.241	-	-	-	11.303	0.917	1.345
12	40.837	46.279	10.239	184.991	-162.808	-110.202	18.348	-	-	7.775	0.874	1.271
13	186.217	108.426	-22.707	271.061	-145.736	-125.012	31.580	2.306	-	3.424	0.945	1.772
14	-84.315	-48.798	-14.631	111.657	-183.928	-144.482	18.722	-	-0.650	13.121	0.694	1.132
15	195.222	120.652	-14.821	280.210	-146.222	-122.182	30.801	2.115	0.085	6.291	0.942	1.900

4.2. Fitting of the Linear Equations of Chloroquines from Ab initio calculation

17 chloroquine compounds have been calculated by ab initio methcd with minimal GLO basis set. The ab initio net charges of chloroquines are presented in table 4.3. Tables 4.4a - 4.4c and 4.5a - 4.5c report the parameters of linear model and fitting characteristics of models from CNDO/2 and ab initio calculations, respectively.

Table 4.3 The net charges for ab inition calculation of atoms in chloroquine drug as used in linear model fitting

Compound no.	Net charges of atoms										
	N1	C2	C3	C4	C5	C6	C7	C8	C9	C10	N2
CQ1	0.4351	-0.1281	0.4958	-0.3669	0.0542	0.2152	0.4160	0.1508	-0.2361	0.6577	0.5446
CQ4	0.4457	-0.1346	0.5084	-0.3727	-0.0076	0.3801	0.0098	0.2580	-0.2670	0.6839	0.5453
CQ5	0.4366	-0.1233	0.4948	-0.3630	0.0616	0.1389	0.5595	0.0774	-0.2305	0.6517	0.5455
CQ6	0.4311	-0.1212	0.4912	-0.3626	0.0506	0.2744	0.4209	0.2094	-0.2410	0.6516	0.5422
CQ7	0.4266	-0.1157	0.4863	-0.3604	0.0048	0.2639	0.3564	0.2131	-0.2325	0.6585	0.5466
CQ8	0.4197	-0.1190	0.4854	-0.3616	0.0667	0.2745	0.3743	0.2018	-0.2935	0.6579	0.5449
CQ9	0.4313	-0.1270	0.4899	-0.3500	0.0417	0.2294	0.4268	0.2250	-0.2426	0.5845	0.5545
CQ10	0.4339	-0.1237	0.4934	-0.3630	-0.0580	0.3168	0.2917	0.1542	-0.2328	0.6718	0.5467
CQ12	0.4042	-0.0806	0.3662	-0.3543	0.0529	0.2197	0.4132	0.1578	-0.2499	0.6617	0.5459
CQ13	0.4232	-0.1150	0.4870	-0.3604	0.1004	0.1846	0.4380	-0.1241	-0.2437	0.6451	0.5464
CQ14	0.3909	-0.0675	0.4414	-0.2347	0.0940	0.1842	0.4103	0.1667	-0.2389	0.6533	0.4446
CQ16	0.3909	-0.0673	0.4412	-0.2346	0.0940	0.1840	0.4102	0.1668	-0.2391	0.6531	0.4449
CQ17	0.3907	-0.0669	0.4406	-0.2336	0.0919	0.1849	0.4097	0.1678	-0.2385	0.6523	0.4432
CQ18	0.4351	-0.1277	0.4955	-0.3669	0.0543	0.2151	0.4163	0.1506	-0.2359	0.6576	0.5440
CQ19	0.4349	-0.1279	0.4958	-0.3669	0.0543	0.2151	0.4162	0.1506	-0.2360	0.6577	0.5440
CQ20	0.6589	0.2565	0.7820	-0.1500	0.3688	0.4930	0.9234	0.3906	0.0109	0.7108	0.6033
CQ21	0.4352	-0.1283	0.4959	-0.3668	0.0541	0.2154	0.4160	0.1508	-0.2361	0.6578	0.5445

Table 4.4a Parameters for linear model and fitting characteristics of the equation including CNDO/2 net charges of atoms N1, C2, C3, C4 and N2 of chloroquine drugs (no. of compounds = 17)

Model	Parameters								D	SD	C max
	pN1	pC2	pC3	pC4	pN2	pC(5-8)	pC(9,10)	pu			
1'	136.274	62.720	-62.522	39.660	-	-	-	-	-1.942	1.188	1.951
2'	97.706	92.541	27.097	-12.278	-232.920	-	-	-	43.727	1.116	1.864
3'	196.281	161.733	60.287	284.766	-248.363	0.324	-181.643	-	58.704	0.849	1.636
4'	78.290	80.351	30.917	-33.590	-264.404	-	-	-0.125	50.030	1.105	1.933
5'	174.608	149.884	69.211	245.606	-368.853	-0.074	-188.174	-0.178	68.735	0.831	1.351

Table 4.4b Parameters for linear model and fitting characteristics of the equation including CNDO/2 net charges of atoms N1, C4, C9, C10 and N2 of chloroquine drugs (no. of compounds = 17)

Model	Parameters								D	SD	C max
	pN1	pC(2,3)	pC4	pC9	pC10	pN2	pC(5-8)	pu			
6'	64.175	-	226.010	-129.946	-103.452	-	-	-	12.507	1.131	1.808
7'	52.153	-	141.302	-110.443	-105.571	-126.633	-	-	32.454	1.071	1.809
8'	117.430	103.334	215.229	-143.566	-167.137	-362.324	1.850	-	84.461	0.915	1.587
9'	53.840	-	119.158	-123.805	-150.517	-248.688	-	-0.412	57.771	1.006	1.730
10'	130.263	117.959	208.481	-167.534	-227.026	-520.841	0.969	-0.458	117.862	1.006	1.730

Table 4.4c Parameters for linear model and fitting characteristics of the equation including CNDO/2 net charges of atoms N1, C2, C3, C4, C9, C10 and N2 of chloroquine drugs (no. of compounds = 17)

Model	Parameters									D	SD	C max
	pN1	pC2	pC3	pC4	pC9	pC10	pN2	pC(5-8)	pu			
11'	202.685	121.366	-31.051	261.551	-153.864	-136.341	-	-	-	7.571	0.988	1.888
12'	188.354	155.211	73.128	252.364	-162.364	-178.153	-291.076	-	-	68.022	0.886	1.750
13'	177.156	143.513	65.481	235.738	-153.473	-170.740	-285.402	1.234	-	66.572	0.883	1.681
14'	143.103	129.655	120.535	222.764	-174.577	-231.750	-516.098	-	-0.449	116.924	0.824	1.371
15'	135.139	121.062	114.197	210.484	-167.697	-225.575	-509.394	0.941	-0.444	115.392	0.822	1.424

Table 4.5a Parameters forlinear model and fitting characteristics of the equation including ab initio net charges of atoms N1, C2, C3, C4 and N2 of chloroquine drugs (no. of compounds = 17)

Model	Parameters								D	SD	C max
	pN1	pC2	pC3	pC4	pN2	pC(5-8)	pC(9-10)	pu			
1"	2.214	-6.980	2.986	16.155	-	-	-	-	6.262	1.237	1.899
2"	3.670	2.119	6.580	-2.712	-18.764	-	-	-	9.987	1.198	1.922
3"	-0.545	-4.616	0.720	-34.683	-58.159	3.178	27.308	-	7.378	0.917	1.524
4"	4.399	13.982	7.405	-0.792	-23.056	-	-	1.373	6.711	0.977	1.814
5"	0.314	-35.169	-6.726	2.611	-27.006	4.443	40.291	-0.244	-2.552	0.848	1.238

Table 4.5b Parameters for linear model and fitting characteristics of the equation including ab initio net charges of atoms N1, C4, C9, C10 and N2 of chloroquine drugs (no. of compounds = 17)

Model	Parameters								D	SD	C max
	pN1	pC(2,3)	pC4	pC9	pC10	pN2	pC(5-8)	pu			
6"	-34.637	-	-0.307	32.483	28.363	-	-	-	6.894	1.044	1.702
7"	2.725	-	-	-30.115	37.620	17.982	-53.753	-	17.368	0.934	1.510
8"	-0.338	-2.271	-39.985	39.176	21.439	-64.028	3.131	-	16.967	0.892	1.440
9"	0.060	-	-24.878	37.859	16.799	-47.735	-	0.271	16.688	0.929	1.637
10"	0.883	-2.295	-38.111	39.013	20.787	-62.263	3.042	0.091	16.725	0.891	1.493

Table 4.5c Parameters for linear model and fitting characteristics of the equation including ab initio net charges of atoms N1, C2, C3, C4, C9, C10 and N2 of chloroquine drugs (no. of compounds = 17)

Model	Parameters										SD	C max
	pN1	pC2	pC3	pC4	pC9	pC10	pN2	pC(5-8)	pu	D		
11"	0.476	-37.525	-7.000	24.927	41.871	35.084	-	-	-	-2.148	0.899	1.416
12"	0.471	-20.935	-3.639	3.918	41.221	27.738	-23.876	-	-	6.904	0.912	1.434
13"	-0.098	-34.242	-7.049	5.503	42.462	35.468	-27.763	4.043	-	0.998	0.845	1.370
14"	0.298	-19.245	-3.464	3.863	40.827	25.932	-24.060	-	0.157	7.447	0.910	1.525
15"	0.171	-36.833	-7.481	5.828	42.963	37.879	-27.776	4.266	-0.172	0.076	0.843	1.266

4.3 Fitting of the Linear Equations of Mefloquines by CNDO/2 Method

A similar approach has been made for mefloquine drugs that have a similar structure to chloroquine. To obtain the correlations, it be necessary to work in consecutive steps as processed with the chloroquines

Table 4.6 report the CNDO/2 net chares of 21 mefloquine compounds that have been used in linear model fitting.

The parameters of various linear models and fitting characteristics of mefloquine compounds are listed in tables 4.7a - 4.7e.

Table 4.6 The net charges for CNDO/2 calculation of atoms in mefloquine drugs as used in linear model fitting

Compounds no.	Net charges of atoms													
	N1	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C13	O27	N2
MF1	-0.0503	0.1387	-0.0578	0.0378	-0.0475	-0.0241	0.0110	-0.0573	0.0888	-0.1230	-0.0169	-0.1337	0.2670	0.1818
MF2	-0.1218	0.1299	-0.0459	0.0289	-0.0357	0.0387	-0.1761	0.0100	0.0639	-0.0982	-0.0373	-0.1356	0.2674	0.1818
MF3	-0.0428	0.1376	-0.0510	0.0327	-0.0423	-0.0077	-0.0097	0.0226	0.0078	-0.1051	-0.0277	-0.1342	0.2672	0.1815
MF4	-0.0465	0.1422	-0.0552	0.0366	-0.0474	-0.0304	0.0610	-0.0483	0.0286	-0.1154	-0.0182	-0.1331	0.2669	0.1813
MF5	-0.1167	0.1314	-0.0347	0.0267	-0.0285	0.0582	-0.1831	0.0355	-0.0005	-0.0787	-0.0430	-0.1370	0.2675	0.1819
MF6	-0.0448	0.1369	-0.0412	0.0322	-0.0348	0.0198	-0.0385	-0.0140	0.0182	-0.0939	-0.0287	-0.1361	0.2674	0.1820
MF7	-0.0455	0.1396	-0.0434	0.0337	-0.0377	0.0091	-0.0048	-0.0123	-0.0183	-0.0843	-0.0271	-0.1353	0.2669	0.1819
MF8	-0.0464	0.1360	-0.0380	0.0300	-0.0323	0.0314	-0.0447	0.0041	-0.0242	-0.0757	-0.0330	-0.1363	0.2672	0.1819
MF9	-0.0250	0.1826	-0.1145	0.0545	-0.0307	0.0248	-0.0290	0.0007	-0.0087	-0.0834	-0.0215	-0.1360	0.2686	0.1830
MF10	-0.0316	0.1850	-0.1182	0.0551	-0.0323	0.0237	-0.0291	-0.0007	-0.0087	-0.0851	-0.0213	-0.1366	0.2676	0.1823
MF11	-0.0339	0.1776	-0.1111	0.0533	-0.0316	0.0258	-0.0320	0.0011	-0.0111	-0.0824	-0.0235	-0.1358	0.2685	0.1827
MF12	-0.0289	0.1827	-0.1154	0.0552	-0.0321	0.0249	-0.0300	0.0005	-0.0093	-0.0836	-0.0218	-0.1357	0.2684	0.1828
MF13	-0.0367	0.1828	-0.1320	0.0602	-0.0450	-0.0271	0.0219	-0.0582	0.0967	-0.1293	-0.0067	-0.1339	0.2675	0.1819
MF14	-0.0263	0.1858	-0.1327	0.0617	-0.0443	-0.0267	0.0236	-0.0574	0.0980	-0.1288	-0.0055	-0.1335	0.2685	0.1826
MF15	-0.0265	0.1899	-0.1361	0.0634	-0.0462	-0.0275	0.0239	-0.0581	0.0988	-0.1298	-0.0048	-0.1332	0.2684	0.1825
MF16	-0.0353	0.1810	-0.1296	0.0607	-0.0454	-0.0262	0.0210	-0.0572	0.0958	-0.1280	-0.0074	-0.1333	0.2684	0.1823
MF17	-0.0177	0.1679	-0.1202	0.0579	-0.0338	0.0130	-0.0225	-0.0165	0.0324	-0.0998	-0.0161	-0.1355	0.2686	0.1830
MF18	-0.0318	0.1817	-0.1171	0.0556	-0.0348	0.0058	0.0060	-0.0142	-0.0053	-0.0918	-0.0177	-0.1358	0.2675	0.1823
MF19	-0.0303	0.1835	-0.1184	0.0562	-0.0351	0.0054	0.0067	-0.0146	-0.0047	-0.0921	-0.0172	-0.1359	0.2673	0.1824
MF20	-0.0392	0.1788	-0.1152	0.0551	-0.0362	0.0060	0.0040	-0.0141	-0.0007	-0.0913	-0.0192	-0.1356	0.2671	0.1820
MF21	-0.0262	0.1848	-0.1189	0.0578	-0.0359	0.0057	0.0070	-0.0139	-0.0044	-0.0917	-0.0167	-0.1350	0.2682	0.1827

Table 4.7a Parameters for linear model and fitting characteristics of the equation including all CNDO/2 net charges of all atoms in quinoline ring and N2 of mefloquine drugs (no. of compounds = 21)

Model	Parameters														SD	C max
	pN1	pC2	pC3	pC4	pC5	pC6	pC7	pC8	pC9	pC10	pC13	pO	pN2	D		
0	26.018	-8.678	2.038	-1.863	0.034	-12.353	9.167	1.964	17.511	-4.085	1208.886	149.899	-1761.860	142.515	0.712	1.788

Table 4.7b Parameters for linear model and fitting characteristics of the equation including CNDO/2 net charges of atoms N1, C2, C3, C4, C13, O and N2 of mefloquine drugs (no. of compounds = 21)

Model	Parameters								u	D	SD	Cmax
	pN1	pC2	pC3	pC4	pC13	pO	pN2	pC(5-10)				
1	-22.319	-26.248	-4.095	-81.958	323.726	-	-	-11.660	-	42.895	0.901	1.515
2	-41.273	-51.704	-3.657	-91.337	-	-	-1223.980	-12.740	-	222.603	0.855	1.841
3	-35.700	-39.942	-4.041	-136.142	-	-235.933	-	-13.589	-	61.132	0.899	1.863
4	-28.460	-32.800	-4.047	-53.464	434.961	-299.433	-	-12.265	-	139.422	0.893	1.576
5	-28.841	-40.369	-3.493	46.846	696.404	-	-1426.988	-10.271	-	357.837	0.838	1.437
6	-15.655	-32.427	-3.006	69.919	675.212	914.733	-2646.970	-7.237	-	332.214	0.808	1.883
7	-19.275	-38.733	-1.712	114.101	445.422	590.899	-2391.873	-6.925	0.488	341.345	0.729	1.536

Table 4.7c Parameters for linear model and fitting characteristics of the equation including CNDO/2 net charges of atoms N1, C4, C9, C10, C13, C and N2 of mefloquine drugs (no. of compounds = 21)

Model	Parameters										SD	C max
	pN1	pC4	pC9	pC10	pC13	pO	pN2	prest*	pu	D		
8	84.034	-86.917	-41.313	-263.264	995.231	-	-	2.018	-	110.309	0.708	1.631
9	84.854	-339.985	-34.142	-226.156	-	-	601.404	-4.398	-	-142.514	0.759	1.570
10	77.963	-325.971	-25.427	-234.259	-	349.165	-	-6.595	-	-123.358	0.758	1.756
11	83.828	-69.066	-42.634	-259.097	1024.813	-	-99.863	2.328	-	133.155	0.768	1.646
12	85.475	-61.545	-45.542	-265.238	1049.538	-88.759	-	3.101	-	141.687	0.707	1.617
13	79.903	-335.086	-27.188	-244.925	-	255.584	203.722	-6.068	-	-136.446	0.757	1.670
14	86.179	-65.283	-46.161	-269.117	1048.011	-122.549	74.947	3.281	-	136.486	0.707	1.600
15	70.519	-65.300	-21.914	-199.239	832.672	65.562	-304.986	-5.070	0.325	131.092	0.676	1.462

*prest = parameter of the grouped atoms C2,C3,C5,C6,C7 and C8

Table 4.7d Parameters for linear model and fitting characteristics of the equation including net charges of atoms N1, C2, C3, C4, C9, C10, C13, O and N2 of mefloquin drugs (no. of compounds = 21)

Model	Parameters											D	SD	C max
	pN1	pC2	pC3	pC4	pC9	pC10	pC13	pO	pN2	pC(5-8)	pu			
16	-11.459	-72.473	2.728	-444.762	21.628	-308.544	-	270.968	-	4.619	-	-95.386	0.668	1.721
17	-6.544	-72.558	2.793	-457.764	15.394	-333.497	-	-	480.748	6.323	-	-112.760	0.669	1.605
18	43.512	-23.783	4.664	-1.615	-36.577	-258.210	1130.462	-	-587.399	10.268	-	243.783	0.693	1.733
19	52.267	-20.159	5.207	-1.592	-46.086	-287.558	1185.920	-328.702	-	12.457	-	229.588	0.694	1.590
20	45.850	-23.131	5.155	-1.632	-39.559	-267.613	1144.816	-115.385	-409.571	10.997	-	243.400	0.639	1.537
21	3.792	-45.879	5.723	-2.358	-0.866	-182.393	832.783	150.654	-1092.737	3.004	0.443	263.654	0.693	1.688

Table 4.7e Parameters for linear model and fitting characteristics of the equation including CNDO/2 net charges of atoms C13, C26, N2 and O of mefloquine drugs (no. of compounds = 21)

Model	Parameters								D	SD	Cmax
	pO	pC13	pC26	pN2	pC4	pN1	prest*	pu			
22	1068.361	1240.410	371.797	-2002.651	134.569	-	-	-	281.919	0.834	1.746
23	1323.750	420.883	195.559	-2657.413	-	23.813	-	-	200.137	0.861	1.896
24	1246.141	1096.113	80.006	-2969.363	24.906	-	-	-	365.311	0.839	2.005
25	926.110	670.610	33.762	-2661.095	67.407	-15.692	-7.238	-	333.637	0.808	1.885
26	641.157	410.946	186.826	-2460.031	101.929	-19.621	-6.916	0.507	349.574	0.725	1.537

*Prest = parameter of the grouped atoms C2, C3, C5, C6, C7, C8, C9 and C10