CHAPTER III

CALCULATIONS

3.1 The Model

To study the relationships between electronic distribution and the pharmacological activity, antimalarial drugs have been chosen. The molecular backbone of chloroquine and mefloquine drugs are illustrated respectively in figures 3.1 and 3.2. Pharmacologically well-characterized drug compounds have been considered for this investigation. Summarizing of chemical derivatives of chloroquine and mefloquine structures and their antimalarial activities are presented in tables 3.1a - 3.1c. The pharmacological activity data have been collected from literature (50,51,52), and a large number of strongly varying modifications (side chains, aromatic substitutes) are described.

Throughout this report, the chloroquine derivatives will be named chloroquines and the mefloquine derivatives will be named mefloquines.

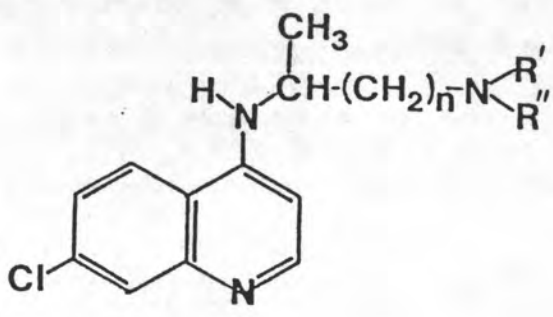


Figure 3.1 Molecular backbone of chloroquine

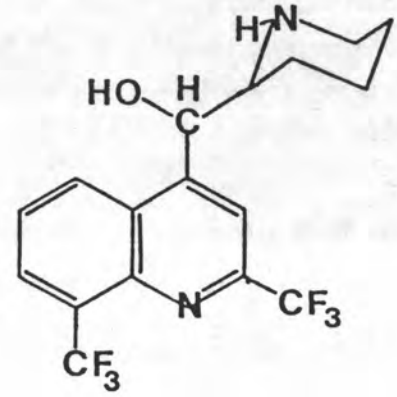
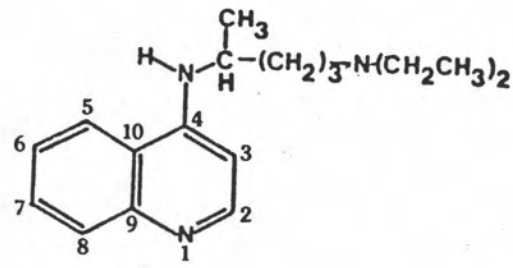


Figure 3.2 Molecular backbone of mefloquine

Table 3.1a Chemical Structure and antimalarial activity of nuclear substitutes of chloroquine drugs

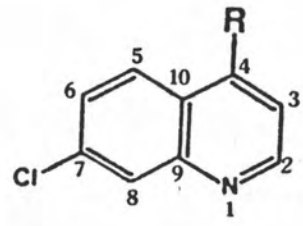


Compound no.	Nuclear substituent (X)	Antimalarial activity*
CQ1	7-Cl	100
CQ2	7-F	50
CQ3	7-CF_3	50
CQ4	7-OCH_3	14
CQ5	7-CH_3	7
CQ6	7-H	7
CQ7	6-Cl	100
CQ8	8-Cl	3
CQ9	5-Cl	3
CQ10	7-Cl,6-CH_3	25
CQ11	7-Cl,3-CH_3	15
CQ12	7-Cl,2-CH_3	10
CQ13	7-Cl,8-NH_2	2

*The values in this table are based defining on chloroquine activity of 100

CQ is the abbreviated name of chloroquines

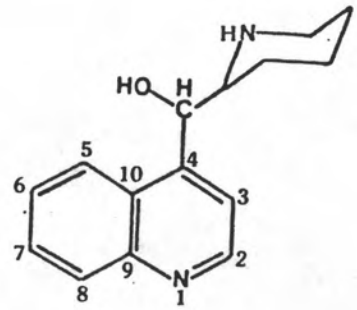
Table 3.1b Chemical Structure and antimalarial activity of different amino side chain of chloroquine drugs



Compound no.	Amino side chain (R)	Antimalarial* activity
CQ14	-NH-C$_6$H$_4$-N(C$_2$H$_5$)$_2$	100
CQ15	-NH-C$_6$H$_4$-N(C$_4$H$_9$)$_2$	25
CQ16	-NH-C$_6$H$_4$-NH-C$_2$H$_5$	100
CQ17	-NH-C$_6$H$_4$-NH-CH(CH$_3$)$_2$	50
CQ18	-NH-CH(CH$_3$)-(CH$_2$)$_3$-NH-CH$_3$	100
CQ19	-NH-CH(CH$_3$)-(CH$_2$)$_3$-NH-C$_2$H$_5$	50
CQ20	-NH-(CH$_2$)$_3$-N(C$_2$H$_5$)$_2$	80
CQ21	-NH-(CH$_2$)$_3$-N(CH$_2$-CH$_2$-OH)$_2$	8
CQ22	-NH-(CH$_2$)$_3$-N(C$_6$H$_{13}$)$_2$	6

*The values in this table are based defining on chloroquine activity of 100

Table 3.1c Chemical Structure and antimalarial activity of mefloquine drugs



Compound no.	Nuclear substituent	Antimalarial* activity
MF1	8-CF_3,2-CF_3	100
MF2	6-OCH_3,8-CF_3,2-CF_3	25
MF3	7-CF_3,2-CF_3	38
MF4	6-CF_3,2-CF_3	12
MF5	6-OCH_3,2-CF_3	6
MF6	6-CH_3,2-CF_3	2
MF7	8-CH_3,2-CF_3	2
MF8	6-CH_3,8-CH_3,2-CF_3	3
MF9	6-CH_3,8-CH_3,4'-CH_3	3
MF10	6-CH_3,8-CH_3,4'-OCH_3	12
MF11	6-CH_3,8-CH_3,4'-Cl	38
MF12	6-CH_3,8-CH_3,4'-F	12
MF13	8-CF_3,4'-H	50
MF14	8-CF_3,4'-CH_3	25
MF15	8-CF_3,4'-OCH_3	37

(continue)

Table 3.1c Chemical structure and antimalarial activity of the mefloquine drugs

Compound no.	Nuclear substituent	Antimalarial activity*
MF16	8-CF_3,4'-Cl	125
MF17	6-CH_3,4'-OCH_3	3
MF18	8-CH_3,4'-H	6
MF19	8-CH_3,4'-CH_3	6
MF20	8-CH_3,4'-Cl	50
MF21	8-CH_3,4'-F	25

*The values in this table are based defining on mefloquine activity of 100.

MF is the abbreviated name of mefloquines

3.2 Methodical Steps

The atomic electron densities and, thereby, net charges have been evaluated by Mulliken population analysis. This method has been very successful in calculating the net charges of atoms (54). The Mulliken's charges have been used in establishing structure-activity correlation models (53).

The calculations are separated into 3 consecutive steps:

3.2.1 Calculation of coordinates of atoms of drug molecules.

3.2.2 Calculation of the electron distribution of cloroquine and mefloquine drugs by the modified CNDO/2 MO SCF program and ab initio program for chloroquine molecules

3.2.3 Fitting of the net electronic charges versus the reactivity of drugs to the numerous linear models

In this work, the chloroquines have been studied first to examine possibilities and limitations of such relationship between electron distribution and their reactivity. A similar approach has been done for another type of antimalarial drugs, mefloquine, and its substituted derivatives which have been investigated in laboratory experiments with respect to their antimalarial activity (51,52,55,56).

According to the above aim of this work the electronic distribution computed by CNDO/2 and ab initio methods are also compared. In practice, ab initio calculations for such molecules can not be performed by the computer of Chulalongkorn University (IBM 3031/08). Therefore, such calculations have been done using the NAS computer of Vienna Technical University. Due to the enormous computer times that would be required for large molecules, only chloroquine analogs have been calculated by ab initio method, using minimal GLO basis set (57). More details of the calculations for each step are given in subsequence sections.

3.2.1 Calculation of the Coordinates of Atoms in Chloroquine and Mefloquine Drugs

The coordinates which are used in this work have been computed by KOGEN program (Appendix I). Molecular geometries were taken from experimental data (58), supported by standard assumptions where necessary and kept constant throughout the calculations. All bond lengths (59) and bond angles are reported in Å and degrees respectively, as shown in tables 3.2a - 3.2b.

Changes of nuclear substituents and side chains of quinoline ring of drug molecules have given the cartesian coordinates as input for CNDO program (Appendix II).

The structure of chloroquine and mefloquine with atomic numbering are illustrated in Figures 3.3 and 3.4 respectively .

The results of coordinate calculations of chloroquines are reported in tables 3.3a - 3.6f and mefloquines are in tables 3.7 - 3.8.

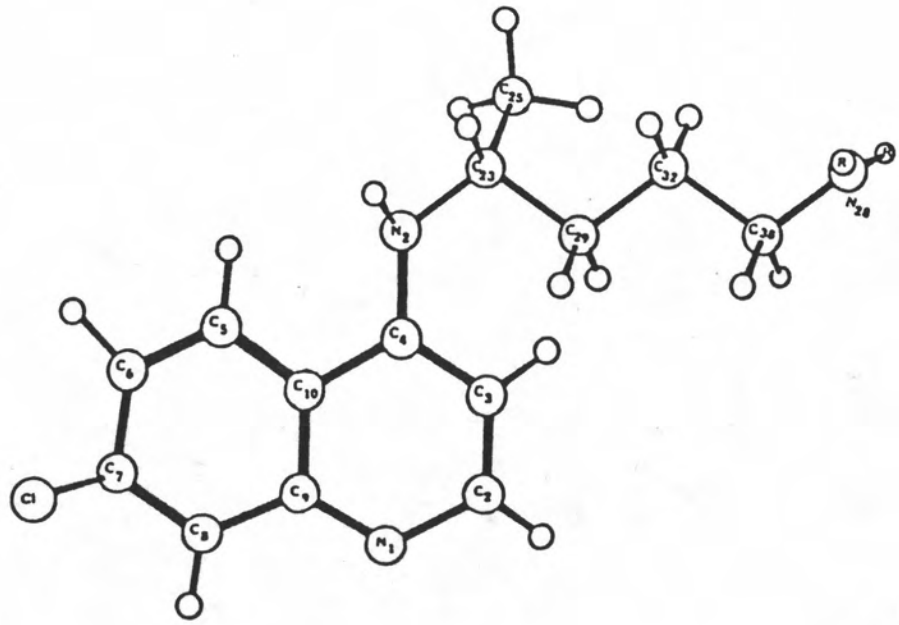


Figure 3.3 Structure of chloroquine with atomic numbering

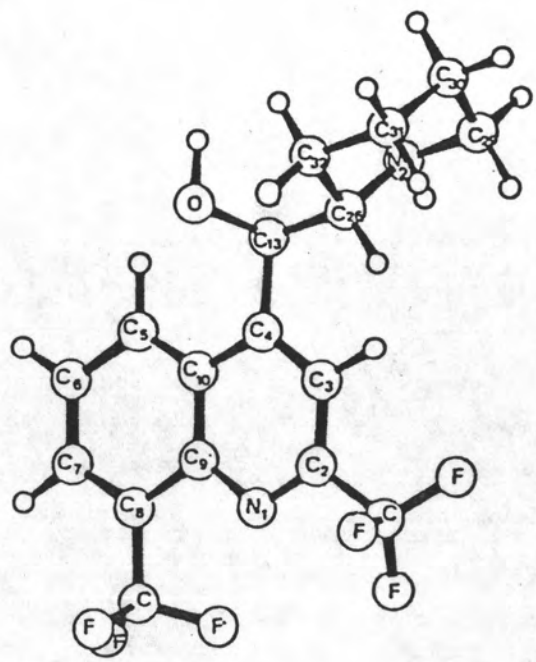


Figure 3.4 Structure of mefloquine with atomic numbering

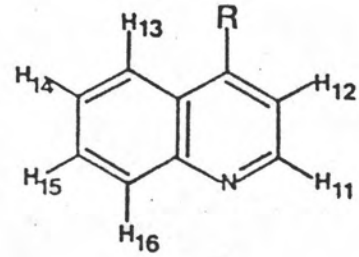
Table 3.2a The geometry parameters of chloroquine drugs

Bond length (Å)		Bond angle (degrees)	
C-C(aliphatic)	1.54	N1$\hat{C}$2C3	121.0
C-H	1.08	C2$\hat{C}$3C4	120.0
C-N(aliphatic)	1.47	C4$\hat{C}$10C5	125.0
C-Cl	1.73	C4$\hat{C}$10C9	114.0
C-F	1.33	C5$\hat{C}$10C9	121.0
N-H	1.08	C6$\hat{C}$5C10	120.1
C-O	1.43	C7$\hat{C}$6C5	118.9
O-H	0.97	C8$\hat{C}$7C6	122.0
N1-C2	1.33	C9$\hat{C}$8C7	119.0
C2-C3	1.37	C10$\hat{C}$9C8	119.0
C3-C4	1.40	C9$\hat{N}$1C2	119.0
C4-C10	1.41	C4$\hat{N}$21H22	120.0
C4-N2	1.46	N1$\hat{C}$9C8	116.0
C5-C10	1.32	tetrahedral	109.5
C5-C6	1.47		
C6-C7	1.34		
C7-C8	1.37		
C8-C9	1.44		
C9-C10	1.40		
C9-N1	1.37		

Table 3.2b The geometry parameters of mefloquine drugs

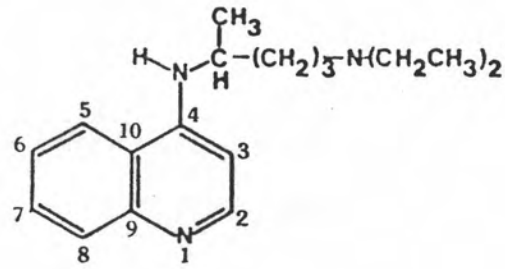
Bond length (Å)		Bond angle (degrees)	
C-C(aliphatic)	1.54	N1$\hat{C}$2C3	121.0
		C2$\hat{C}$3C4	120.0
		C4$\hat{C}$10C5	125.0
C-Cl	1.73	C4$\hat{C}$10C9	114.0
C-H	1.08	C5$\hat{C}$10C9	121.0
N-H	1.08	C6$\hat{C}$5C10	120.1
C-O	1.43	C7$\hat{C}$6C5	118.9
O-H	0.97	C8$\hat{C}$7C6	122.0
N1-C2	1.33	C9$\hat{C}$8C7	119.0
C2-C3	1.38	C1$\hat{O}$C9C8	119.0
C3-C4	1.40	C9$\hat{N}$1C2	119.0
C4-C10	1.41	C4$\hat{C}$13O25	109.5
C4-C13	1.46	N1$\hat{C}$9C8	116.0
C-N(aliphatic)	1.47	C13$\hat{O}$25H26	111.0
C-F	1.33	tetrahedral	109.5
C5-C10	1.32		
C5-C6	1.47		
C6-C7	1.34		
C7-C8	1.37		
C8-C9	1.44		
C9-C10	1.40		
C9-N1	1.37		

Table 3.3 The cartesian coordinates (Å) of atoms in quinoline ring of chloroquine drugs



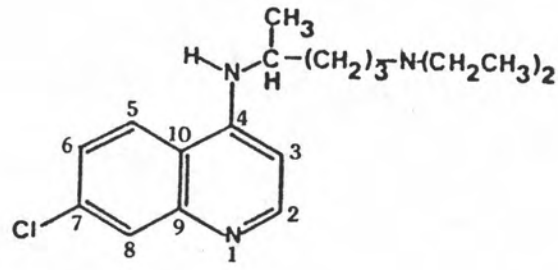
Atom	X	Y	Z
N1	-2.765	0.072	-0.000
C2	-2.080	1.212	-0.000
C3	-0.700	1.212	-0.000
C4	0.000	0.000	0.000
C5	-0.107	-2.422	0.000
C6	-0.928	-3.645	0.000
C7	-2.263	-3.528	0.000
C8	-2.885	-2.308	0.000
C9	-2.080	-1.114	0.000
C10	-0.685	-1.236	0.000
H11	-2.621	2.151	-0.000
H12	-0.158	2.151	-0.000
H13	0.975	-2.498	0.000
H14	-0.450	-4.628	0.000
H15	-0.452	-4.628	0.000
H16	-3.961	-2.176	-0.000

Table 3.4 The cartesian coordinates (Å) of nuclear substituent in quinoline ring of chloroquine drugs



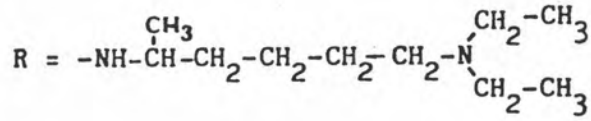
Nuclear substituent (X)	Atom	X	Y	Z
7-Cl	Cl15	-3.237	-4.913	0.000
7-F	F15	-3.027	-4.620	0.000
$7\text{-}CF_3$	C15	-3.132	-4.769	0.000
	F17	-2.358	-5.854	0.000
	F18	-3.902	-4.773	1.088
	F19	-3.902	-4.773	-1.088
$7\text{-}OCH_3$	O15	-3.055	-4.659	0.000
	C17	-2.201	-5.836	0.000
	H18	-1.215	-5.566	0.000
	H19	-2.481	-6.420	0.882
	H20	-2.481	-6.420	-0.882
$7\text{-}CH_3$	C15	-3.132	-4.769	0.000
	H17	-2.505	-5.649	0.000
	H18	-3.756	-4.773	0.882
	H19	-3.756	-4.773	-0.882
5-Cl	Cl13	1.579	-2.537	0.000
6-Cl	Cl14	-0.185	-5.163	0.000
8-Cl	Cl16	-4.573	-2.219	0.000

Table 3.5 The cartesian coordinates (Å) of additional nuclear substituent in quinoline ring of chloroquine drugs



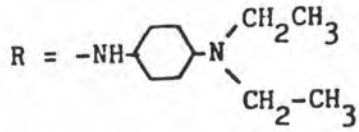
Nuclear substituent (X)	Atom	X	Y	Z
6-CH_3	C14	-0.288	-5.018	0.000
	H17	0.787	-4.915	0.000
	H18	-0.579	-5.560	0.882
	H19	-0.597	-5.560	-0.882
3-CH_3	C13	0.057	2.524	0.000
	H17	-0.644	3.346	0.000
	H18	0.679	2.582	0.882
	H19	0.679	2.582	-0.882
2-CH_3	C11	-2.837	2.524	0.000
	H17	-2.136	3.345	0.000
	H18	-3.459	2.582	-0.882
	H19	-3.459	2.582	0.082
8-NH_2	N16	-4.343	-2.231	0.000
	H17	-4.685	-3.171	0.000
	H18	-4.610	-1.739	0.828

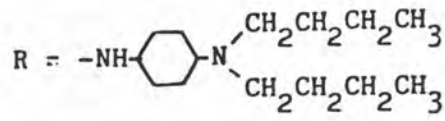
Table 3.6a The cartesian coordinates (Å) of atoms in amino side chain of chloroquine drugs, CQ1 - CQ13



Atom	X	Y	Z
N2	1.460	0.000	0.000
H22	2.000	-0.801	-0.482
C23	2.195	1.091	0.656
H24	2.816	1.595	-0.069
C25	3.081	0.513	1.776
H26	3.783	-0.190	1.353
H27	3.621	1.314	2.258
H28	2.460	0.009	2.502
C29	1.195	2.094	1.260
H30	0.573	1.591	1.986
H31	0.573	2.500	0.476
C32	1.965	2.237	1.948
H33	2.586	3.741	1.222
H34	2.586	2.831	2.733
C35	0.965	4.240	2.552
H36	0.343	3.737	3.278
H37	0.343	4.646	1.767
N3	1.700	5.331	3.208
C39	2.523	4.721	4.262
H40	3.207	4.012	3.819
H41	1.885	4.212	4.969
C42	3.322	5.818	4.990
H43	3.208	4.012	3.820
H44	1.885	4.212	4.969
H45	3.083	5.490	4.773
C46	2.523	5.976	2.176
H47	1.885	6.363	1.395
H48	3.207	5.254	1.756
C49	3.321	7.133	2.804
H50	3.083	6.788	2.617
H51	1.885	6.362	1.395
H52	3.208	5.254	1.756

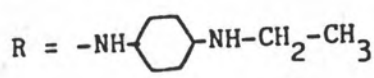
Table 3.6b The cartesian coordinates (Å) of atoms in amino side chain of chloroquine drugs, CQ14 and CQ15

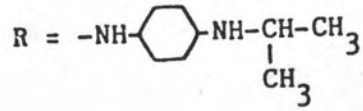




Atom (CQ14)	X	Y	Z	Atom (CQ15)	X	Y	Z
N2	1.460	0.000	0.000	C40	1.808	-3.408	-3.254
H22	1.784	-0.363	0.997	H41	0.853	-3.835	-4.984
C23	1.890	-0.481	-1.321	H42	2.539	-3.659	-4.500
H24	2.969	-0.497	-1.365	C43	2.257	-3.975	-6.614
C25	1.346	0.460	-2.412	H44	3.212	-3.548	-6.884
H26	1.727	1.457	-2.251	H45	1.526	-3.725	-7.368
H27	0.267	0.476	-2.369	C46	1.808	-0.766	-6.216
C28	1.796	-0.044	-3.796	H47	2.539	-0.090	-5.800
H29	1.415	0.616	-4.562	H48	0.853	-0.266	-6.234
H30	2.875	-0.060	-3.840	C49	2.258	-1.206	-7.621
C31	1.252	-1.466	-4.028	H50	1.526	-1.883	-8.038
H32	0.173	-1.451	-3.984	H51	3.212	-1.706	-7.554
C33	1.796	-2.408	-2.937	C52	2.389	-5.506	-6.514
N3	1.682	-1.947	-5.348	H53	1.434	-5.933	-6.245
H35	1.415	-3.405	-3.100	H54	3.121	-5.757	-5.761
H36	2.875	-2.424	-2.980	C55	2.839	-6.072	-7.871
C37	1.346	-1.906	-1.553	H56	3.794	-5.646	-8.144
H38	0.267	-1.890	-1.509	H57	2.108	-5.822	-8.628
H39	1.727	-2.567	-0.788	H58	2.931	-7.146	-7.804
C40	1.808	-3.408	-5.254	C59	2.389	0.030	-8.529
H41	0.853	-3.836	-4.985	H60	3.121	0.707	-8.113
H42	2.539	-3.659	-4.500	H61	1.435	0.530	-8.598
C43	2.257	-3.975	-6.614	C62	2.839	-0.410	-9.935
H44	3.212	-3.548	-6.884	H63	2.108	-1.086	-10.352
H45	1.526	-3.725	-7.368	H64	3.794	-0.910	-9.868
H46	2.350	-5.048	-6.544	H65	2.931	0.457	-10.572
H47	1.808	-0.766	-6.216				
H48	2.539	-0.090	-5.800				
H49	0.853	-0.266	-6.284				
C50	2.258	-1.206	-7.621				
H51	1.526	-1.883	-8.038				
H52	3.212	-1.706	-7.554				
H53	2.350	-0.339	-8.258				

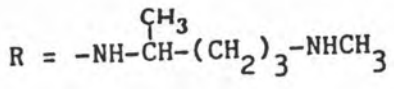
Table 3.6c The cartesian coordinates (Å) of atoms in amino side chain of chloroquine drugs, CQ16 and CQ17

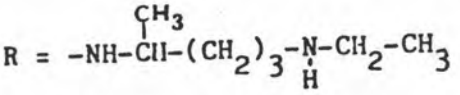




Atom (CQ16)	X	Y	Z	Atom (CQ17)	X	Y	Z
(coordinates of atoms N2-H39 are the same as in CQ14)							
C40	1.808	-3.408	-5.254	C40	2.672	-3.009	-5.118
H41	0.853	-3.836	-4.985	H41	2.218	-3.808	-4.551
H42	2.539	-3.659	-4.500	C42	3.163	-3.556	-6.471
C43	2.258	-3.975	-6.164	H43	3.618	-2.758	-7.039
H44	3.212	-3.548	-6.884	H44	2.326	-3.958	-7.023
H45	1.526	-3.725	-7.368	H45	3.890	-4.336	-6.302
H46	2.350	-5.048	-6.544	C46	3.866	-2.437	-4.333
H47	1.768	-1.136	-5.944	H47	3.523	-2.053	-3.383
				H48	4.322	-1.638	-4.900
				H49	4.594	-3.217	-4.163

Table 3.6d The cartesian coordinates (Å) of atoms in amino side chain of chloroquine drugs, CQ18 and CQ19





Atom (CQ18)	X	Y	Z	Atom (CQ19)	X	Y	Z
N2	1.460	0.000	0.000	N2	1.460	0.000	0.000
H22	2.000	-0.801	-0.485	H22	2.000	-0.801	-0.482
C23	2.195	1.091	0.656	C23	2.195	1.091	0.656
H24	2.816	1.595	-0.069	H24	2.816	1.595	-0.692
C25	3.081	0.513	1.776	C25	3.081	0.513	1.776
H26	3.783	-0.190	1.353	H26	3.783	-0.190	1.353
H27	3.621	1.314	2.258	H27	3.621	1.314	2.258
H28	2.460	0.009	2.502	H28	2.460	0.009	2.503
C29	1.195	2.094	1.260	C29	1.195	2.094	1.260
H30	0.574	1.591	1.986	H30	0.574	1.591	1.986
H31	0.574	2.500	0.476	H31	0.574	2.500	0.476
C32	1.965	3.237	1.948	C32	1.965	3.237	1.948
H33	2.586	3.741	1.222	H33	2.586	3.741	1.222
H34	2.586	2.832	2.733	H34	2.586	2.832	2.733
C35	0.965	4.240	2.552	C35	0.965	4.240	2.552
H36	0.343	3.737	3.278	H36	0.343	3.737	3.278
H37	0.343	4.646	1.767	H37	0.343	4.646	1.767
N3	1.700	5.331	3.208	N3	1.700	5.331	3.208
H39	2.266	5.774	2.499	H39	2.256	5.774	2.499
C40	2.523	4.721	4.263	C40	2.523	4.721	4.262
H41	3.208	4.012	3.820	H41	3.208	4.012	3.820
H42	1.885	4.212	4.969	H42	1.885	4.212	4.969
H43	3.083	5.490	4.773	C43	3.321	5.818	4.990
				H44	3.927	5.370	5.764
				H45	2.638	6.527	5.433
				H46	3.961	6.328	4.284

Table 3.6e The cartesian coordinates (Å) of atoms in amino side chain of chloroquine drugs, CQ20 and CQ21

R = $-NH-(CH_2)_3-N(CH_2CH_3)_2$ R = $-NH-(CH_2)_3-N-(CH_2CH_2-OH)_2$

Atom (CQ20)	X	Y	Z	Atom (CQ21)	X	Y	Z
N2	1.460	0.000	0.000	N2	1.460	0.000	0.000
H22	2.000	-0.801	-0.482	H22	2.000	-0.801	-0.782
C23	2.195	1.091	0.656	C23	2.195	1.091	0.656
H24	1.934	2.031	0.193	H24	1.934	2.031	0.193
H25	1.934	1.122	1.704	H25	1.934	1.122	1.704
C26	3.709	0.850	0.512	C26	3.709	0.850	0.512
H27	3.971	-0.089	0.975	H27	3.971	-0.089	0.975
H28	3.971	0.820	-0.536	H28	3.971	0.820	-0.536
C29	4.479	1.993	1.199	C29	4.479	1.993	1.199
H30	4.219	2.933	0.736	H30	4.219	2.933	0.736
H31	4.219	2.024	2.247	H31	4.219	2.024	2.247
N3	5.541	1.824	1.098	N3	5.541	1.824	1.098
C33	6.092	1.722	2.457	C33	6.092	1.722	2.457
C34	6.092	2.978	0.371	C34	6.092	2.977	0.371
H35	5.900	3.881	0.930	H35	5.901	3.881	0.930
H36	5.622	3.049	-0.599	H36	5.623	3.049	-0.599
C37	7.611	2.795	0.193	C37	7.611	2.795	0.193
H38	7.803	1.892	-0.366	H38	7.803	1.892	-0.366
H39	8.081	2.724	1.163	H39	8.081	2.724	1.163
H40	8.015	3.642	-0.341	O40	8.146	3.917	-0.514
H41	5.901	2.639	2.994	H41	9.104	3.828	-0.639
H42	5.623	0.898	2.975	H42	5.901	2.639	2.994
C43	7.611	1.479	2.379	H43	5.623	0.898	2.975
H44	8.081	2.303	1.862	C44	7.611	1.480	2.379
H45	7.803	0.562	1.843	H45	8.081	2.303	1.862
H46	8.015	1.404	3.378	H46	7.083	0.562	1.846
				O47	8.146	1.380	3.701
				H48	9.104	1.227	3.680

Table 3.6f The cartesian coordinates (Å) of atoms in amino side chain of chloroquine drugs, CQ22

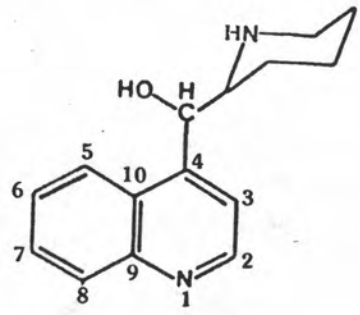
$$R = -NH-(CH_2)_3-N-(CH_2CH_2CH_2CH_2CH_2CH_3)_2$$

Atom (CQ22)	X	Y	Z	Atom (CQ22)	X	Y	Z
(coordinates of atoms N2-H31 are the same as in CQ20)							
N3	5.541	1.824	1.098	C51	10.297	5.035	-1.514
C33	6.092	1.722	2.457	H52	9.828	5.107	-2.483
C34	6.092	2.977	0.371	H53	10.106	5.939	-0.954
H35	5.901	3.881	0.930	C54	11.826	4.852	-1.692
H36	5.623	3.049	-0.599	H55	12.296	4.781	-0.722
C37	7.611	2.795	0.193	H56	12.018	3.949	-2.252
H38	7.803	1.892	-0.366	H57	12.230	5.699	-2.226
H39	8.081	2.724	1.163	C58	8.191	1.371	3.812
H40	5.901	2.639	2.994	H59	7.722	0.548	4.330
H41	5.623	0.898	2.975	H60	8.000	2.289	4.349
C42	7.611	1.479	2.379	C61	9.720	1.128	3.734
H43	8.081	2.303	1.862	H62	9.912	0.210	3.198
H44	7.803	0.562	1.843	H63	10.190	1.951	3.217
C45	8.188	4.003	-0.568	C64	10.301	1.020	5.167
H46	7.997	4.907	-0.009	H65	10.110	1.937	5.704
H47	7.718	4.075	-1.538	H66	9.832	0.196	5.685
C48	9.716	3.820	-0.747	C67	11.829	0.776	5.089
H49	9.908	2.916	-1.307	H68	12.021	-0.142	4.553
H50	10.187	3.748	0.223	H69	12.300	1.599	4.572
				H70	12.234	0.701	6.088

Table 3.7 The cartesian coordinates (Å) of mefloquine, MF1

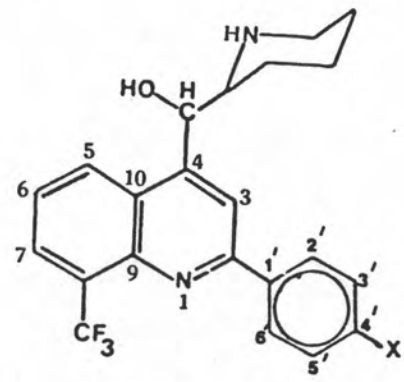
Atom	X	Y	Z
N1	-2.765	0.072	0.000
C2	-2.080	1.212	0.000
C3	-0.700	1.212	0.000
C4	0.000	0.000	0.000
C5	-0.106	-2.422	0.000
C6	-0.928	-3.645	0.000
C7	-2.263	-3.528	0.000
C8	-2.885	-2.307	0.000
C9	-2.080	-1.114	0.000
C10	-0.685	-1.236	0.000
C11	-2.840	2.528	0.000
H12	-.157	2.151	0.000
H14	.974	-2.498	0.000
H15	-.470	-4.627	0.000
H16	-2.885	-4.416	0.000
C17	-4.393	-2.122	0.000
F18	-4.830	-2.069	-1.244
F19	-4.961	-3.138	0.622
F20	-4.699	-0.999	0.622
F21	-3.059	2.909	-1.244
F22	-3.993	2.370	0.622
F23	-2.126	3.448	0.622
C13	1.510	0.000	0.000
O25	1.987	-0.673	-1.167
H26	2.957	-0.686	-1.189
H24	1.867	-0.504	0.873
C27	2.024	1.451	0.000
H33	1.192	2.125	0.000
N28	2.846	1.684	1.208
H42	2.285	1.526	2.033
C29	3.340	3.079	1.208
H40	3.935	3.242	2.081
H41	2.509	3.752	1.208
C30	4.196	3.321	0.048
H38	5.028	2.649	0.049
H39	4.553	4.330	0.048
C31	3.341	3.080	-1.307
H36	2.509	3.753	-1.307
H37	3.936	3.249	-2.180
C32	2.827	1.629	-1.308
H34	3.659	0.955	-1.308
H35	2.233	1.461	-2.182

Table 3.8a The cartesian coordinates (Å) of nuclear substituent in quinoline ring of mefloquine drugs



Nuclear substituent	Atom	X	Y	Z
2-CF_3	C	-3.506	2.910	-1.244
	F1	-3.993	2.371	-1.244
	F2	-3.993	2.371	0.622
	F3	-2.126	3.448	0.622
6-CF_3	C	-0.286	-5.023	0.000
	F1	-1.235	-5.955	0.000
	F2	0.470	-5.160	-1.806
	F3	0.470	-5.160	1.086
7-CF_3	C	-3.135	-4.774	0.000
	F1	-2.363	-5.856	0.000
	F2	-3.903	-4.778	1.086
	F3	-3.903	-4.778	-1.086
8-CF_3	C	1.510	0.000	0.000
	F1	-4.831	-2.069	-1.244
	F2	-4.962	-3.139	0.622
	F3	-4.699	-0.999	0.622
6-CH_3	C	-0.285	-5.023	0.000
	H1	-1.056	-5.780	0.000
	H2	0.327	-5.135	-0.881
	H3	0.327	-5.135	0.881
8-CH_3	C	1.510	0.000	0.000
	H1	-4.876	-3.089	0.000
	H2	-4.689	-1.573	0.881
	H3	-4.689	-1.573	-0.881
6-OCH_3	O	-0.354	-4.877	0.000
	C	-1.292	-1.957	0.000
	H1	-0.765	-6.888	0.000
	H2	-1.907	-5.896	0.873
	H3	-1.907	-5.895	-0.873
6-Cl	Cl	-0.180	-5.172	0.000

Table 3.8b The cartesian coordinates (Å) of nuclear substituent in quinoline ring of mefloquine drugs



Nuclear substituent	Atom	X	Y	Z
2-phen	C1'	-1.510	0.000	0.000
	C2'	-2.143	3.736	0.000
	C3'	-2.840	4.943	0.000
	C4'	-4.234	4.943	0.000
	C5'	-4.931	3.736	0.000
	C6'	-4.234	2.529	0.000
	H2'	-4.774	1.594	0.000
	H3'	-6.011	3.736	0.000
	H5'	-2.299	5.878	0.000
	H6'	-1.063	3.736	0.000
4'-OCH_3	O	-4.914	6.121	0.000
	C	-6.434	5.330	0.000
	H1	-6.950	6.829	0.000
	H2	-6.711	5.321	-0.882
	H3	-6.711	5.321	0.882
4'-Cl	Cl	-5.089	6.424	0.000
4'-F	F	-4.899	6.095	0.000
4'-H	H	-1.063	3.736	0.000
4'-CH_3	C	-5.004	6.277	0.000
	H1	-6.065	6.080	0.000
	H2	-4.743	6.844	0.881
	H3	-4.743	6.844	-0.881

3.2.2 Calculation of the Electron Distribution of Cloroquine and Mefloquine Drugs

The calculations of the electron distribution in our study uses Mulliken's atomic populations based on the standardized semiempirical CNDO/2 MO SCF procedure as electronic structure data, within a series of rather rigid topology in order to avoid lengthy gecmetry optimizations.

The results of the atomic charges of chloroquines are reported in tables 3.9a - 3.9k, and mefloquines are in tables 3.10a - 3.10g.

Tables 3.11 and 3.12 report the dipole moments and total energies of chloroquines and mefloquines, respectively.

Table 3.9a Atomic charges of atoms in chloroquine drugs, CQ1 and CQ2

Atom (CQ1)	Atomic charges		Atom (CQ2)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.1953	7.4351	N1	5.2014	-
C2	3.8725	5.8719	C2	3.8687	-
C3	4.1075	6.4958	C3	4.1141	-
C4	3.8402	5.6331	C4	3.8352	-
C5	3.9805	6.0542	C5	3.9624	-
C6	4.0160	6.2152	C6	4.0784	-
C7	3.8820	6.4160	C7	3.7439	-
C8	4.0304	6.1508	C8	4.1011	-
C9	3.8812	5.7639	C9	3.8655	-
C10	4.0121	6.6577	C10	4.0283	-
H11	1.0181	0.7365	H11	1.0194	-
H12	0.9693	0.7522	H12	0.9708	-
H13	1.0048	0.7090	H13	1.0060	-
H14	0.9876	0.6844	H14	0.9802	-
C115	7.1834	16.8112	F15	7.2146	-
H16	0.9789	0.6632	H16	0.9721	-
N2	5.2286	7.5446	N2	5.2291	-
H18	0.9041	0.6396	H18	0.9045	-
C19	3.8629	6.1087	C19	3.8629	-
H20	1.0286	0.7743	H20	1.0288	-
C21	4.0327	6.5251	C21	4.0325	-
H22	0.9961	0.8066	H22	0.9964	-
H23	0.9912	0.8093	H23	0.9914	-
H24	0.9905	0.7911	H24	0.9907	-
C25	4.0161	6.3976	C25	4.0162	-
H26	0.9972	0.7443	H26	0.9971	-
H27	0.9737	0.8398	H27	0.9728	-
C28	4.0098	6.5384	C28	4.0099	-
H29	0.9966	0.7641	H29	0.9968	-
H30	0.9960	0.7671	H30	0.9962	-
C31	0.9045	6.1903	C31	3.9045	-
H32	1.0178	0.7810	H32	1.0178	-
H33	1.0191	0.7870	H33	1.0189	-
N3	5.1603	7.5166	N3	5.1603	-
C35	3.8929	6.2386	C35	3.8927	-
H36	1.0249	0.8392	H36	1.0249	-
H37	1.0155	0.7872	H37	1.0156	-
C38	4.0643	6.5599	C38	4.0643	-
H39	1.0017	0.8063	H39	1.0017	-
H40	0.9885	0.7892	H40	0.9886	-
H41	0.9526	0.8052	H41	0.9526	-
C42	3.8931	6.2883	C42	3.8931	-
H43	1.0157	0.8201	H43	1.0157	-
H44	1.0246	0.8729	H44	1.0246	-
H45	1.0642	0.8169	H45	4.0642	-
			H46	0.9526	-
			H47	1.0018	-
			H48	0.9886	-

Table 3.9b Atomic charges of atoms in chloroquine drugs, CQ3 and CQ4

Atom (CQ3)	Atomic charges		Atom (CQ4)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.1943	-	N1	5.2044	7.4457
C2	3.8716	-	C2	3.8690	5.8654
C3	4.1066	-	C3	4.1166	6.5084
C4	3.8406	-	C4	3.8349	5.6273
C5	3.9807	-	C5	3.9641	5.9924
C6	4.0066	-	C6	4.0868	6.3801
C7	4.0171	-	C7	3.7941	6.0098
C8	4.0232	-	C8	4.0978	6.2580
C9	3.8817	-	C9	3.8667	5.7330
C10	4.0093	-	C10	4.0314	6.6839
H11	1.0171	-	H11	1.0219	0.7389
H12	0.9681	-	H12	0.9727	0.7547
H13	1.0046	-	H13	1.0113	0.7155
H14	0.9903	-	H14	0.9840	0.7044
C15	3.4022	-	O15	6.2189	8.1583
F16	7.2244	-	C16	3.8882	6.1960
F17	7.2187	-	H17	0.9940	0.9303
F18	7.2187	-	H18	1.0089	0.8548
H19	0.9845	-	H19	1.0089	0.8547
N2	5.2285	-	H20	0.9811	0.6601
H21	0.9036	-	N21	5.2295	7.5453
C22	3.8629	-	H22	0.9056	0.6407
H23	1.0281	-	C23	3.8627	6.1084
C24	4.0326	-	H24	1.0296	0.7754
H25	0.9958	-	C24	4.0323	6.5253
H26	0.9907	-	H26	0.9974	0.8078
H27	0.9904	-	H27	0.9915	0.8099
C28	4.0162	-	H28	0.9913	0.7915
H29	0.9972	-	C29	4.0159	6.3966
H30	0.9741	-	H30	0.9972	0.7441
C31	4.0099	-	H31	0.9721	0.8385
H32	0.9963	-	C32	4.0082	6.5388
H33	0.9956	-	H33	1.0005	0.7648
C34	3.9046	-	H34	1.0008	0.7678
H35	1.0177	-	C35	3.8948	6.1809
H36	1.0189	-	H36	1.0253	0.7806
N3	5.1601	-	H37	1.0267	0.7859
C38	3.8927	-	N3	5.1255	7.5261
H39	1.0249	-	C39	3.8578	6.2354
H40	1.0155	-	H40	1.0272	0.8391
C41	4.0643	-	C41	4.0349	6.5593
H42	1.0015	-	H42	0.9891	0.7875
H43	0.9884	-	H43	0.9955	0.8068
H44	0.9525	-	H44	0.9870	0.7894
C45	3.8930	-	H45	1.0147	0.8053
H46	1.0156	-	C46	3.8558	6.2863
H47	1.0247	-	H47	1.0219	0.8208
C48	4.0642	-	H48	1.0237	0.8732
			H49	0.9879	0.8179

Table 3.9c Atomic charges of atoms in chloroquine drugs, CQ5 and CQ6

Atom (CQ5)	Atomic charges		Atom (CQ6)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.2015	7.4366	N1	5.1983	7.4311
C2	3.8733	5.8768	C2	3.8750	5.8782
C3	4.1128	6.4948	C3	4.1097	6.4912
C4	3.8397	5.6370	C4	3.8423	5.6374
C5	3.9795	6.0616	C5	3.9842	6.0506
C6	4.0346	6.1389	C6	4.0195	6.2745
C7	3.9330	6.5595	C7	3.9643	6.4209
C8	4.0590	6.0774	C8	4.0413	6.2094
C9	3.8805	5.7695	C9	3.8836	5.7590
C10	4.0280	6.6517	C10	4.0149	6.6515
H11	1.0229	0.7391	H11	1.0222	0.7377
H12	0.9741	0.7540	H12	0.9734	0.7531
H13	1.0129	0.7179	H13	1.0118	0.7149
H14	1.0065	0.7001	H14	1.0055	0.6943
C15	4.0245	6.3786	H15	1.0151	0.6726
H16	1.0018	0.7999	H16	0.9959	0.6714
H17	0.9900	0.7876	N2	5.2295	7.5452
H18	0.9900	0.7871	H18	0.9052	0.6392
H19	0.9975	0.6771	C19	3.8628	6.1080
N2	5.2295	7.5455	H20	1.0310	0.7751
H21	0.9052	0.6395	C21	4.0324	6.5201
C22	3.8629	6.1078	H22	0.9969	0.8069
H23	1.0302	0.7756	H23	0.9926	0.8101
C24	4.0324	6.5251	H24	0.9909	0.7912
H25	0.9970	0.8073	C25	4.0167	6.3980
H26	0.9926	0.8156	H26	0.9969	0.7445
H27	0.9910	0.7913	H27	0.9721	0.8399
C28	4.0168	6.3977	C28	4.0099	6.5381
H29	0.9969	0.7444	H29	0.9972	0.7643
H30	0.9716	0.8395	H30	0.9967	0.7671
C31	4.0098	6.5383	C31	3.9046	6.1870
H32	0.9973	0.7646	H32	1.0179	0.7806
H33	0.9967	0.7674	H33	1.0189	0.7860
C34	3.9046	6.1869	N3	5.1606	7.5258
H35	1.0179	0.7806	C35	3.8930	6.2356
H36	1.0189	0.7860	H36	1.0245	0.8392
N3	5.1607	7.5261	H37	1.0156	0.7874
C38	3.8928	6.2354	C38	4.0642	6.5592
H39	1.0246	0.8391	H39	1.0020	0.8064
H40	1.0157	0.7875	H40	0.9889	0.7893
C41	4.0643	6.5592	H41	0.9527	0.8052
H42	1.0021	0.8066	C42	3.8932	6.2864
H43	0.9889	0.7894	H43	1.0157	0.8207
H44	0.9527	0.8033	H44	1.0244	0.8733
C45	3.8930	6.2863	H45	0.9882	0.8175
H46	1.0157	0.8208			
H47	1.0244	0.8732			
H48	0.9889	0.8178			

Table 3.9d Atomic charges of atoms in chloroquine drugs, CQ7 and CQ8

Atom (CQ7)	Atomic charges		Atom (CQ8)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.1978	7.4266	N1	5.1863	7.1497
C2	3.8701	5.8843	C2	3.8713	5.8810
C3	4.1100	6.4863	C3	4.1092	6.4854
C4	3.8372	5.6396	C4	3.8386	5.6384
C5	3.9712	6.0048	C5	3.9741	6.0667
C6	3.9416	6.2639	C6	4.0226	6.2745
C7	3.9577	6.3564	C7	3.9562	6.3742
C8	4.0421	6.2131	C8	3.9626	6.2018
C9	3.8766	5.7645	C9	3.8728	5.7065
C10	4.0170	6.6585	C10	4.0160	6.6579
H11	1.0186	0.7372	H11	1.0163	0.7366
H12	0.9690	0.7520	H12	0.9693	0.7529
H13	0.9973	0.7067	H13	1.0066	0.7142
C114	7.1727	16.8236	H14	0.9987	0.6903
H15	0.9978	0.6620	H15	0.9980	0.6634
H16	0.9888	0.6649	C116	7.1654	16.7874
N2	5.2287	7.5466	N2	5.2284	7.5449
H18	0.9028	0.6395	H18	0.9040	0.6382
C19	3.8629	6.1075	C19	3.8629	6.1079
H20	1.0283	0.7750	H20	1.0284	0.7747
C21	4.0327	6.5251	C21	4.0326	6.5250
H22	0.9954	0.8065	H22	0.9962	0.8067
H23	0.9912	0.8103	H23	0.9911	0.8100
H24	0.9902	0.7911	H24	0.9905	0.7909
C25	4.0160	6.3980	C25	4.0163	6.3985
H26	0.9972	0.7444	H26	0.9969	0.7443
H27	0.9740	0.8407	H27	0.9733	0.8400
C28	4.0099	6.5381	C28	4.0099	6.5380
H29	0.9965	0.7641	H29	0.9965	0.7642
H30	0.9958	0.7668	H30	0.9960	0.7661
C31	3.9044	6.1869	C31	3.9045	6.1869
H32	1.0179	0.7806	H32	1.0176	0.7805
H33	1.0192	0.7863	H33	1.0188	0.7860
N3	5.1602	7.5258	N3	5.1601	7.5257
C35	3.8928	6.2357	C35	3.8928	6.2357
H36	1.0247	0.8392	H36	1.0249	0.8393
H37	1.0156	0.7873	H37	1.0155	0.7873
C38	4.0643	6.5591	C38	4.0643	6.5591
H39	1.0016	0.8063	H39	1.0017	0.8064
H40	0.9985	0.7893	H40	0.9884	0.7892
H41	0.9526	0.8052	H41	0.9526	0.8523
C42	3.8930	6.2864	C42	3.8933	6.2864
H43	1.0158	0.8207	H43	1.0155	0.8207
H44	1.0246	0.8733	H44	1.0246	0.8734
H45	0.9886	0.8174	H45	0.9885	0.8173

Table 3.9e Atomic charges of atoms in chloroquine drugs, CQ9 and CQ10

Atom (CQ9)	Atomic charges		Atom (CQ10)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.1970	7.4312	N1	5.1896	7.4339
C2	3.8725	5.8730	C2	3.8777	5.8763
C3	4.1103	6.4899	C3	4.1042	6.4934
C4	3.8352	5.6500	C4	3.8465	5.6370
C5	3.9048	6.0417	C5	4.0043	5.9420
C6	4.0073	6.2294	C6	3.9725	6.3168
C7	3.9673	6.4268	C7	3.8990	6.2917
C8	4.0325	6.2250	C8	4.0248	6.1542
C9	3.8825	5.7574	C9	3.8900	5.7673
C10	4.0087	6.5845	C10	4.0074	6.6718
H11	1.0192	0.7362	H11	1.0189	0.7375
H12	0.9681	0.7496	H12	0.9702	0.7532
Cl13	7.1997	16.8320	H13	1.0047	0.7118
H14	0.9903	0.6852	C14	4.0154	6.4089
H15	1.0071	0.6660	H15	1.0003	0.8011
H16	0.9905	0.6697	H16	0.9810	0.7869
N2	5.2352	7.5545	H17	0.9809	0.7869
H18	0.8643	0.6167	Cl18	7.1899	16.8074
C19	3.8626	6.1110	H19	0.9801	0.6663
H20	1.0299	0.7757	N2	5.2291	7.5467
C21	4.0320	6.5256	H21	0.9047	0.6412
H22	0.9936	0.8086	C22	3.8629	6.1076
H23	0.9935	0.8097	H23	1.0289	0.7751
H24	0.9894	0.7915	C24	4.0324	6.5252
C25	4.0160	6.3963	H25	0.9964	0.8074
H26	0.9975	0.7468	H26	0.9915	0.8099
H27	0.9753	0.8424	H27	0.9908	0.7914
C28	4.0016	6.5378	C28	4.0161	6.3977
H29	0.9969	0.7650	H29	0.9972	0.7443
H30	0.9958	0.7678	H30	0.9735	0.8397
C31	3.9047	6.1868	C31	4.0097	6.5383
H32	1.0181	0.7812	H32	0.9967	0.7643
H33	1.0194	0.7868	H33	0.9960	0.7672
N3	5.1606	7.5266	C34	3.9046	6.1869
C35	3.8928	6.2352	H35	1.0177	0.7851
H36	1.0243	0.8393	H36	1.0189	0.7851
H37	1.0157	0.7877	N37	5.1602	7.5258
C38	4.0642	6.5592	C38	3.8927	6.2356
H39	1.0018	0.8068	H39	1.0247	0.8393
H40	0.9889	0.7895	H40	1.0156	0.7874
H41	0.9527	0.8054	C41	4.0643	6.5592
C42	3.8930	6.2861	H42	1.0017	0.8065
H43	1.0159	0.8212	H43	0.9885	0.7893
H44	1.0243	0.8734	H44	0.9526	0.8053
H45	0.9889	0.8180	C45	3.8929	6.2864
			H46	1.0157	0.8207
			H47	1.0246	0.8734
			H48	0.9885	0.8175

Table 3.9f Atomic charges of atoms in chloroquine drugs, CQ11 and CQ12

Atom (CQ11)	Atomic charges		Atom (CQ12)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.1794	-	N1	5.2196	7.4042
C2	3.8899	-	C2	3.8405	5.9194
C3	4.0363	-	C3	4.1216	6.3662
C4	3.8653	-	C4	3.8365	5.6457
C5	3.9776	-	C5	3.9779	6.0529
C6	4.0235	-	C6	4.0206	6.2197
C7	3.8810	-	C7	3.8794	6.4132
C8	4.0364	-	C8	4.0387	6.1578
C9	3.8873	-	C9	3.8783	5.7501
C10	4.0127	-	C10	4.0180	6.6617
H11	1.0142	-	C11	4.0444	6.4783
C12	4.0084	-	H12	0.9962	0.8014
H13	1.0000	-	H13	0.9783	0.7708
H14	0.9927	-	H14	0.9786	0.7725
H15	0.9940	-	H15	0.9706	0.7567
H16	0.9949	-	H16	1.0060	0.7101
H17	0.9885	-	H17	0.9886	0.6855
C118	7.1841	-	C118	7.1857	16.8138
H19	0.9796	-	H19	0.9802	0.6647
N2	5.2430	-	N2	5.2289	7.5459
H21	0.9050	-	H21	0.9040	0.6399
C22	3.8615	-	C22	3.8628	6.1084
H23	1.0264	-	H23	1.0287	0.7751
C24	4.0381	-	C24	4.0324	6.5249
H25	0.9955	-	H25	0.9961	0.8069
H26	0.9925	-	H26	0.9914	0.8100
H27	0.9862	-	H27	0.9905	0.7911
C28	4.0156	-	C28	4.0161	6.3994
H29	0.9779	-	H29	0.9973	0.7436
H30	1.0020	-	H30	0.9734	0.8405
C31	4.0074	-	C31	4.0102	6.5381
H32	0.9950	-	H32	0.9964	0.7644
H33	0.9945	-	H33	0.9957	0.7669
C34	3.9050	-	C34	3.9046	6.1865
H35	1.0181	-	H35	1.0179	0.7805
H36	1.0172	-	H36	1.0193	0.7874
N3	5.1600	-	N3	5.1602	7.5259
C38	3.8929	-	C38	3.8926	6.2357
H39	1.0253	-	H39	1.0247	0.8391
H40	1.0150	-	H40	1.0156	0.7873
C41	4.0641	-	C41	4.0643	6.5591
H42	1.0015	-	H42	1.0015	0.8063
H43	0.9882	-	H43	0.9885	0.7893
H44	0.9527	-	H44	0.9525	0.8052
C45	3.8928	-	C45	3.8929	6.2864
H46	1.0154	-	H46	1.0158	0.8211
H47	1.0248	-	H47	1.0246	0.8732
C48	4.0643	-	H48	0.9885	0.8173
H49	0.9525	-			
H50	1.0016	=			
H51	0.9884				

Table 3.9g Atomic charges of atoms in chloroquine drugs, CQ13 and CQ14

Atom (CQ13)	Atomic charges		Atom (CQ14)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.1841	7.4232	N1	5.1885	7.3909
C2	3.8816	5.8850	C2	3.8749	5.9325
C3	4.1009	6.4870	C3	4.0810	6.4414
C4	3.8478	5.6397	C4	3.8551	5.7653
C5	4.0096	6.1004	C5	3.9398	6.0940
C6	3.9968	6.1846	C6	4.0618	6.1842
C7	3.9289	6.4380	C7	3.8633	6.4103
C8	3.9079	5.8759	C8	4.0669	6.1667
C9	3.9173	5.7563	C9	3.8724	5.7611
C10	3.9984	6.6451	C10	4.0412	6.6533
H11	1.0187	0.7378	H11	1.0163	0.7311
H12	0.9700	0.7537	H12	0.9936	0.6805
H13	1.0051	0.7107	H13	0.9846	0.7092
H14	0.9889	0.6877	H14	0.9900	0.6889
C115	7.8191	16.8267	C115	7.1869	16.8153
N16	5.2055	7.4780	H16	0.9816	0.6886
H17	0.9016	0.7158	N2	5.2159	7.4456
H18	0.9052	0.6980	H18	0.9222	0.6724
N2	5.2288	7.5464	C19	3.8727	6.1347
H20	0.9041	0.6386	H20	1.0134	0.7289
C21	3.8630	6.1071	C21	4.0016	6.4501
H22	1.0291	0.7754	H22	1.0014	0.7444
C23	4.0325	6.5251	H23	0.9968	0.7434
H24	0.9962	0.8069	C24	3.9987	6.4808
H25	0.9917	0.8111	H25	1.0044	0.7523
H26	0.9907	0.7915	H26	0.9990	0.7695
C27	4.0160	6.3981	C27	3.8849	6.1021
H28	0.9974	0.7451	H28	1.0328	0.7874
H29	0.9738	0.8398	C29	4.0041	6.4172
C30	4.0099	6.5382	N3	5.2182	7.6986
H31	0.9966	0.7642	H31	1.0059	0.7563
H32	0.9959	0.7672	H32	0.9990	0.7770
C33	3.9046	6.1869	C33	4.0099	6.4597
H34	1.0179	0.7812	H34	0.9698	0.7524
H35	1.0190	0.7859	H35	1.0055	0.8195
N3	5.1602	7.5261	C36	3.8556	6.0726
C37	3.8928	6.2355	H37	1.0223	0.8426
H38	1.0247	0.8390	H38	1.0212	0.8347
H39	1.0156	0.7877	C39	4.0354	6.5619
C40	4.0643	6.5592	H40	0.9885	0.7993
H41	1.0016	0.8066	H41	0.9876	0.7961
H42	0.9886	0.7895	H42	0.9950	0.8122
H43	0.9525	0.8051	C43	3.8557	6.1344
C44	3.8932	6.2864	H44	1.0215	0.8641
H45	1.0156	0.8207	H45	1.0229	0.8740
H46	1.0245	0.8731	H46	0.9953	0.8231
H47	0.9886	0.8177			

Table 3.9h Atomic charges of atoms in chloroquine drugs, CQ15 and CQ16

Atom (CQ15)	Atomic charges		Atom (CQ16)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.1884	-	N1	5.1885	7.3909
C2	3.8744	-	C2	3.8751	5.9327
C3	4.0810	-	C3	4.0810	6.4412
C4	3.8549	-	C4	3.8553	5.7654
C5	3.9396	-	C5	3.9398	6.0939
C6	4.0617	-	C6	4.0618	6.1840
C7	3.8630	-	C7	3.8632	6.4102
C8	4.0671	-	C8	4.0672	6.1668
C9	3.8721	-	C9	3.8724	5.7609
C10	4.0410	-	C10	4.0414	6.6531
H11	1.0161	-	H11	1.0163	0.7313
H12	0.9933	-	H12	0.9937	0.6805
H13	0.9844	-	H13	0.9848	0.7091
H14	0.9898	-	H14	0.9901	0.6888
Cl15	7.1864	-	Cl15	7.1870	16.8154
H16	0.9813	-	H16	0.9816	0.6687
N17	5.2157	-	N2	5.2160	7.4449
H18	0.9220	-	H18	0.9221	0.6714
C19	3.8726	-	C19	3.8729	6.1346
H20	1.0133	-	H20	1.0133	0.7286
C21	4.0014	-	C21	3.9983	6.4691
H22	1.0015	-	H22	1.0014	0.7435
C23	0.9968	-	H23	0.9965	0.7419
C24	3.9990	-	C24	4.0036	6.4670
H25	1.0045	-	H25	1.0065	0.7654
H26	0.9991	-	H26	0.9987	0.7659
C27	3.8850	-	C27	3.8808	6.1127
H28	1.0334	-	H28	1.0349	0.7978
C29	4.0040	-	C29	4.0020	6.4317
N3	5.2246	-	N3	5.2647	7.7204
H31	1.0063	-	H31	1.0054	0.7556
H32	0.9991	-	H32	0.9988	0.7772
C33	4.0097	-	C33	4.0102	6.4595
H34	0.9699	-	H34	0.9697	0.7524
H35	1.0057	-	H35	1.0052	0.8191
C36	3.8609	-	C36	3.8494	6.1005
H37	1.0021	-	H37	1.0237	0.8438
H38	1.0209	-	H38	1.0228	0.8346
C39	4.0069	-	C39	4.0359	6.5615
H40	0.9962	-	H40	0.9897	0.8010
H41	0.9952	-	H41	0.9888	0.7982
C42	3.8613	-	H42	0.9937	0.8122
H43	1.0210	-	H43	0.8690	0.5968
H44	1.0225	-			
C45	4.0067	-			
H46	0.9952	-			
H47	0.9960	-			
C48	3.9808	-			

Table 3.9i Atomic charges of atoms in chloroquine drugs, CQ17 and CQ18

Atom (CQ17)	Atomic charges		Atom (CQ18)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.1882	7.3907	N1	5.1947	7.4349
C2	3.8751	5.9331	C2	3.8728	5.8721
C3	4.0809	6.4406	C3	4.1076	6.4958
C4	3.8554	5.7664	C4	3.8047	5.6331
C5	3.9390	6.0919	C5	3.9809	6.0543
C6	4.0620	6.1849	C6	4.0161	6.2151
C7	3.8630	6.4097	C7	3.8822	6.4162
C8	4.0671	6.1678	C8	4.0338	6.1505
C9	3.8727	5.7615	C9	3.8811	5.7640
C10	4.0411	6.6523	C10	4.0125	6.6576
H11	1.0163	0.7312	H11	1.0182	0.7365
H12	0.9938	0.6806	H12	0.9697	0.7523
H13	0.9849	0.7115	H13	1.0048	0.7089
H14	0.9902	0.6889	H14	0.9876	0.6844
Cl15	7.1869	16.8152	Cl15	7.1836	16.8119
H16	0.9817	0.6688	H16	0.9798	0.6632
N17	5.2157	7.4432	N2	5.2288	7.5440
H18	0.9222	0.6716	H18	0.9040	0.6403
C19	3.8739	6.1398	C19	3.8630	6.1079
H20	1.0162	0.7309	H20	1.0284	0.7751
C21	3.9990	6.4723	C21	4.0330	6.5254
H22	1.0012	0.7427	H22	0.9958	0.8066
H23	0.9957	0.7428	H23	0.9910	0.8097
C24	4.0019	6.4804	H24	0.9906	0.7911
H25	1.0033	0.7591	C25	4.0163	6.4054
H26	0.9994	0.7659	H26	0.9970	0.7436
C27	3.8880	6.1832	H27	0.9734	0.8395
H28	1.0229	0.7452	C28	4.0080	6.5264
C29	4.0474	6.3891	H29	1.0001	0.7738
N3	5.1950	7.4128	H30	0.9956	0.7705
H31	1.0058	0.7510	C31	3.9036	6.2093
H32	0.9462	0.8502	H32	1.0102	0.7965
C33	4.0077	6.4274	H33	1.0184	0.7853
H34	0.9720	0.7572	N3	5.1769	7.5361
H35	1.0077	0.8193	H35	0.9256	0.7227
H36	0.9371	0.7276	C36	3.9240	6.3103
C37	3.8736	6.2908	H37	1.0158	0.8788
H38	1.0102	0.7505	H38	1.0029	0.8313
C39	4.0294	6.4620	H39	1.0111	0.8184
H40	0.9913	0.8095			
H41	0.9940	0.7891			
H42	0.9951	0.8117			
C43	4.0496	6.4938			
H44	0.9787	0.8761			
H45	0.9956	0.8002			
H46	0.9950	0.8093			

Table 3.9j Atomic charges of atoms in chloroquine drugs, CQ19 and CQ20

Atom (CQ19)	Atomic charges		Atom (CQ20)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.2026	7.4351	N1	5.1970	7.6589
C2	3.8720	5.8723	C2	3.8690	6.2526
C3	4.1078	6.4955	C3	4.0909	6.7820
C4	3.8347	5.6331	C4	3.8392	5.8500
C5	3.9766	6.0543	C5	3.9796	6.3688
C6	4.0167	6.2151	C6	4.0173	6.4930
C7	3.8832	6.4163	C7	3.8812	6.9234
C8	4.0376	6.1506	C8	4.0350	6.3906
C9	3.8830	5.7641	C9	3.8794	6.0109
C10	4.0048	6.6576	C10	4.0138	6.7108
H11	1.0179	0.7366	H11	1.0169	1.0202
H12	0.9698	0.7520	H12	0.9923	0.8855
H13	1.0051	0.7089	H13	1.0051	0.9124
H14	0.9877	0.6845	H14	0.9881	0.9971
Cl15	7.1830	16.8114	Cl15	7.1845	17.5885
H16	0.9787	0.6633	H16	0.9791	0.9611
N17	5.2269	7.5440	N2	5.2223	7.6033
H18	0.9047	0.6406	H18	0.9005	0.7733
C19	3.8632	6.1078	C19	3.8779	6.0981
H20	1.0288	0.7753	H20	1.0189	0.9430
C21	4.0331	6.5253	H21	1.0208	0.9297
H22	0.9960	0.8069	C22	4.0623	6.3612
H23	0.9913	0.8097	H23	0.9954	0.8864
H24	0.9906	0.7911	H24	0.9950	0.9001
C25	4.0160	6.4071	C25	3.7180	5.9095
H26	0.9971	0.7437	H26	1.1108	0.9808
H27	0.9735	0.8399	H27	1.1109	0.9777
C28	4.0082	6.5230	N3	5.1571	8.1587
H29	1.0006	0.7750	C29	3.8781	6.0893
H30	0.9961	0.7688	C30	3.8780	6.0774
C31	3.9059	6.2060	H31	1.0160	1.0177
H32	1.0112	0.7966	H32	1.0089	0.9622
H33	1.0194	0.7873	C33	4.0728	6.6578
N3	5.1840	7.5111	H34	0.9866	0.9556
H35	0.9254	0.7247	H35	0.9505	1.0184
C36	3.8966	6.2587	H36	0.9968	1.1390
H37	1.0237	0.8445	H37	1.0160	1.0195
H38	1.0104	0.8011	H38	1.0089	0.9546
C39	4.0296	6.5530	C39	4.0728	6.6590
H40	0.9960	0.8089	H40	0.9505	1.0186
H41	0.9900	0.7902	H41	0.9866	0.9546
H42	0.9929	0.8093	H42	0.9968	1.1375

Table 3.9k Atomic charges of atoms in chloroquine drugs, CQ21 and CQ22

Atom (CQ21)	Atomic charges		Atom (CQ22)	Atomic charges	
	CNDO/2	ab initio		CNDO/2	ab initio
N1	5.1962	7.4352	N1	5.1965	-
C2	3.8690	5.8718	C2	3.8686	-
C3	4.0905	6.4959	C3	4.0906	-
C4	3.8393	5.6332	C4	3.8392	-
C5	3.9795	6.0541	C5	3.9795	-
C6	4.0169	6.2154	C6	4.0166	-
C7	3.8812	6.4160	C7	3.8809	-
C8	4.0347	6.1508	C8	4.0345	-
C9	3.8794	5.7639	C9	3.8792	-
C10	4.0138	6.6578	C10	4.0135	-
H11	1.0164	0.7364	H11	1.0166	-
H12	0.9922	0.7519	H12	0.9919	-
H13	1.0053	0.7091	H13	1.0048	-
H14	0.9879	0.6846	H14	0.9879	-
C115	7.1837	16.8115	C115	7.1835	-
H16	0.9788	0.6632	H16	0.9789	-
N17	5.2221	7.5445	N2	5.2219	-
H18	0.9002	0.6399	H18	0.9003	-
C19	3.8779	6.1088	C19	3.8778	-
H20	1.0181	0.7744	H20	1.0188	-
H21	1.0200	0.8070	H21	1.0206	-
C22	4.0612	6.5251	C22	4.0629	-
H23	0.9945	0.8092	H23	0.9955	-
H24	0.9941	0.7912	H24	0.9951	-
C25	3.7222	6.3966	C25	3.7151	-
H26	1.1059	0.7446	H26	1.1125	-
H27	1.1059	0.8399	H27	1.1125	-
N28	5.1507	6.5394	N3	5.1650	-
C29	3.9024	6.2887	C29	3.8828	-
C30	3.9022	6.2815	C30	3.8828	-
H31	1.0036	0.7750	H31	1.0159	-
H32	0.9967	0.8330	H32	1.0086	-
C33	3.9052	6.1350	C33	4.0474	-
H34	1.0138	0.9000	H34	0.9943	-
H35	0.9775	0.9008	H35	0.9579	-
O36	6.2533	8.2469	H36	1.0159	-
H37	0.8650	0.7612	H37	1.0085	-
H38	1.0036	0.8754	C38	4.0484	-
H39	0.9966	0.8208	H39	0.9578	-
H40	0.9775	0.8124	H40	0.9940	-
			C41	0.9859	-
			H42	1.0042	-
			H43	1.0035	-

(continue)

Table 3.9k Atomic charges of atoms in chloroquine drugs, CQ21 and CQ22

	Atom (CQ22)	Atomic charges	
		CNDO/2	ab initio
	C44	3.9880	-
	H45	1.0019	-
	H46	1.0047	-
	C47	3.9847	-
	H48	1.0022	-
	H49	1.0028	-
	C50	4.0145	-
	H51	0.9962	-
	H52	0.9958	-
	H53	1.0009	-
	C54	3.9869	-
	H55	1.0031	-
	H56	1.0039	-
	C57	3.9879	-
	H58	1.0091	-
	H59	1.0048	-
	C60	3.9845	-
	H61	1.0028	-
	H62	1.0022	-
	C63	4.0414	-
	H64	0.9958	-
	H65	0.9962	-
	H66	1.0009	-

Table 3.10a Atomic charges of atoms in mefloquine drugs, MF1, MF2 and MF3

Atomic charges (CNDO/2)					
MF1		MF2		MF3	
N1	5.1953	N1	5.1299	N1	5.1376
C2	3.9422	C2	3.9541	C2	3.9490
C3	4.0378	C3	4.0289	C3	4.0327
C4	3.9525	C4	3.9643	C4	3.9577
C5	3.9759	C5	4.0387	C5	3.9923
C6	4.0110	C6	3.8239	C6	3.9903
C7	3.9427	C7	4.0100	C7	4.0226
C8	4.0888	C8	4.0639	C8	4.0078
C9	3.8770	C9	3.9018	C9	3.8949
C10	3.9831	C10	3.9627	C10	3.9723
C11	3.4024	C11	3.4016	C11	3.4028
H12	0.9777	H12	0.9783	H12	0.9780
H13	0.9917	H13	0.9803	H13	0.9906
H14	0.9909	H14	0.9860	H14	0.9846
H15	0.9992	C15	3.3846	F15	7.2121
C16	3.3830	F16	7.2153	F16	7.2143
F17	7.2176	F17	7.2220	F17	7.2186
F18	7.2228	F18	7.2154	C18	3.8658
F19	7.2176	F19	7.2130	O19	6.2672
F20	7.2114	F20	7.2124	H26	0.8544
F21	7.2110	F21	7.2197	H24	1.0129
F22	7.2189	C22	3.8644	C22	3.9230
C23	3.8663	O23	6.2674	H23	1.0133
O24	6.2670	H26	0.8553	N2	5.1815
H26	0.8544	H24	1.0139	H25	0.9337
H24	1.0127	C26	3.9228	C26	3.9022
C27	3.9229	H27	1.0132	H27	1.0171
H28	1.0128	N28	5.1818	H28	1.0205
N2	5.1818	H29	0.9336	C29	3.9956
H30	0.9336	C30	3.9022	H30	0.9971
C31	3.9023	H31	1.0174	H31	1.0037
H32	1.0170	H32	1.0204	C32	3.9820
H33	1.0203	C33	3.9953	H33	1.0018
C34	3.9955	H34	0.9974	H34	1.0121
H35	0.9973	H35	1.0041	C35	3.9910
H36	1.0037	C36	3.9820	H36	0.9996
C37	3.9820	H37	1.0017	H37	0.9965
H38	1.0016	H38	1.0124	C38	3.3994
H39	1.0121	C39	3.9912	H39	0.9806
C40	3.9908	H40	0.9997	F40	7.2219
H41	1.0000	H41	0.9965	F41	7.2166
H42	0.9965	O42	6.2041	F42	7.2163
		C43	3.8687		
		H44	0.9958		
		H45	1.0054		
		H46	1.0053		

Table 3.10b Atomic charges of atoms in mefloquine drugs, MF4, MF5 and MF6

Atomic charges (CNDO/2)					
MF4		MF5		MF6	
N1	5.1422	N1	5.1314	N1	5.1369
C2	3.9448	C2	3.9653	C2	3.9588
C3	4.0366	C3	4.0267	C3	4.0322
C4	3.9526	C4	3.9715	C4	3.9652
C5	3.9696	C5	4.0582	C5	4.0190
C6	4.0610	C6	3.8169	C6	3.9615
C7	3.9517	C7	4.0355	C7	3.9860
C8	4.0286	C8	3.9995	C8	4.0182
C9	3.8846	C9	3.9213	C9	3.9061
C10	3.9818	C10	3.9570	C10	3.9713
C11	3.4031	C11	3.4036	C11	3.4040
H12	0.9776	H12	0.9826	H12	0.9829
H13	0.9872	H13	0.9857	H13	0.9981
H14	0.9955	H14	0.9956	H14	1.0106
F15	7.2119	F15	7.2162	F15	7.2156
F16	7.2143	F16	7.2181	F16	7.2176
F17	7.2183	F17	7.2215	F17	7.2213
C18	3.8669	C18	3.8630	C18	3.8639
O19	6.2669	O19	6.2675	O19	6.2674
H20	0.8531	H20	0.8580	H20	0.8580
H21	1.0119	H21	1.0156	H21	1.0153
C22	3.9225	C22	3.9236	C22	3.9236
H23	1.0135	H23	1.0129	H23	1.0124
N24	5.1813	N2	5.1819	N2	5.1820
H25	0.9336	H25	0.9341	H25	0.9341
C26	3.9023	C26	3.9023	C26	3.9024
H27	1.0169	H27	1.0187	H27	1.0186
H28	1.0107	H28	1.0210	H28	1.0209
C29	3.9954	C29	3.9954	C29	3.9955
H30	0.9969	H30	0.9979	H30	0.9980
H31	1.0038	H31	1.0052	H31	1.0051
C32	3.9820	C32	3.9822	C32	3.9822
H33	1.0019	H33	1.0022	H33	1.0021
H34	1.0120	H34	1.0136	H34	1.0135
H35	3.9911	C35	3.9907	C35	3.9907
H36	0.9992	H36	1.0003	H36	1.0006
H37	0.9964	H37	0.9968	H37	0.9968
H38	0.9838	O38	6.2072	H38	0.9919
C39	3.3943	C39	3.8676	C39	4.0228
F40	7.2240	H40	0.9996	H40	0.9954
F41	7.2178	H41	1.0076	H41	0.9860
F42	7.2189	H42	1.0071	H42	0.9873
		H43	0.9906		

Table 3.10c Atomic charges of atoms in mefloquine drugs, MF7, MF8 and MF9

Atomic charges (CNDO/2)					
MF7		MF8		MF9	
N1	5.1396	N1	5.1360	N1	5.1410
C2	3.9566	C2	3.9620	C2	3.9481
C3	4.0337	C3	4.0300	C3	4.0359
C4	3.9623	C4	3.9677	C4	3.9550
C5	4.0091	C5	4.0314	C5	3.9848
C6	3.9952	C6	3.9553	C6	3.9269
C7	3.9877	C7	4.0041	C7	3.9632
C8	3.9817	C8	3.9758	C8	4.0260
C9	3.9157	C9	3.9243	C9	3.8907
C10	3.9729	C10	3.9670	C10	3.9794
C11	3.4042	C11	3.4041	C11	3.4032
H12	0.9826	H12	0.9834	H12	0.9789
H13	0.9984	H13	0.9991	H13	0.9835
H14	0.9999	H14	1.0115	H14	0.9930
H15	1.0106	C15	4.0193	F15	7.2129
C16	4.0184	F16	7.2161	F16	7.2153
F17	7.2154	F17	7.2183	F17	7.2293
F18	7.2178	F18	7.2214	C18	3.8664
F19	7.2209	C19	3.8637	O19	6.2667
C20	3.8647	O20	6.2672	H20	0.8543
O21	6.2669	H21	0.8586	H21	1.0125
H22	0.8576	H22	1.0155	C22	3.9229
H23	1.0145	C23	3.9238	H23	1.0133
C24	3.9236	H24	1.0125	N2	5.1815
H25	1.0126	N2	5.1819	H25	0.9338
N26	5.1819	H26	0.9341	C26	3.9024
H27	0.9341	C27	3.9026	H27	1.0174
C28	3.9025	H28	1.0187	H28	1.0207
H29	1.0185	H29	1.0209	C29	3.9957
H30	1.0209	C30	3.9951	H30	0.9972
C31	3.9954	H31	0.9981	H31	1.0042
H32	0.9979	H32	1.0054	C32	3.9821
H33	1.0051	C33	3.9821	H33	1.0020
C34	3.9823	H34	1.0022	H34	1.0124
H35	1.0021	H35	1.0137	C35	3.9909
H36	1.0134	C36	3.9905	H36	0.9996
C37	3.9906	H37	1.0006	H37	0.9966
H38	1.0004	H38	0.9969	H38	0.9844
H39	0.9968	H39	0.9985	C139	7.1577
H40	0.9984	H40	0.9834		
H41	0.9841	H41	0.9834		
H42	0.9841	C42	4.0234		
		H43	0.9958		
		H44	0.9856		
		H45	0.9869		

Table 3.10d Atomic charges of atoms in mefloquine drugs, MF10, MF11 and MF12

Atomic charges (CNDO/2)					
MF10		MF11		MF12	
N1	5.1850	N1	5.1776	N1	5.1827
C2	3.8818	C2	3.8889	C2	3.8846
C3	4.0551	C3	4.0533	C3	4.0552
C4	3.9677	C4	3.9684	C4	3.9679
C5	4.0237	C5	4.0258	C5	4.0249
C6	3.9709	C6	3.9680	C6	3.9700
C7	3.9993	C7	4.0011	C7	4.0005
C8	3.9913	C8	3.9889	C8	3.9907
C9	3.9149	C9	3.9176	C9	3.9164
C10	3.9787	C10	3.9765	C10	3.9782
C11	4.0177	C11	3.9833	C11	4.0082
H12	0.9937	H12	0.9930	H12	0.9941
H13	1.0033	H13	1.0027	H13	1.0033
H14	1.0163	H14	1.0156	H14	1.0163
C15	3.8634	C15	3.8642	C15	3.8643
O16	6.2676	O16	6.2685	O16	6.2684
H17	0.8613	H17	0.8614	H17	0.8618
H18	1.0177	H18	1.0178	H18	1.0180
C19	3.9246	C19	3.9244	C19	3.9245
H20	1.0112	H20	1.0129	H20	1.0125
N2	5.1823	N21	5.1827	N21	5.1828
H22	0.9343	H22	0.9350	H22	0.9350
C23	3.9022	C23	3.9018	C23	3.9018
H24	1.0199	H24	1.0206	H24	1.0208
H25	1.0229	H25	1.0247	H25	1.0248
C26	3.9949	C26	3.9960	C26	3.9959
H27	0.9980	H27	0.9984	H27	0.9985
H28	1.0068	H28	1.0069	H28	1.0071
C29	3.9818	C29	3.9825	C29	3.9825
H30	1.0039	H30	1.0045	H30	1.0046
H31	1.0149	H31	1.0151	H31	1.0153
C32	3.9905	C32	3.9911	C32	3.9911
H33	1.0005	H33	1.0008	H33	1.0009
H34	0.9970	H34	0.9977	H34	0.9976
C35	3.9793	C35	4.0024	C35	3.9820
C36	4.0497	C36	3.9846	H36	4.0486
C37	3.8115	C37	3.9176	H37	3.7712
C38	4.0607	C38	3.9852	H38	4.0492
C39	3.9738	C39	3.9974	C39	3.9770
H40	1.0008	H40	0.9945	H40	0.9955
H41	0.9947	H41	0.9908	H41	0.9837
H42	0.9925	H42	0.9911	H42	0.9840
H43	1.0040	H43	0.9990	H43	1.0001
C44	4.0231	C44	4.0241	C44	4.0237
H45	0.9980	H45	0.9978	H45	0.9983
H46	0.9897	H46	0.9893	H46	0.9899
H47	0.9910	H47	0.9905	H47	0.9911

Table 3.10e Atomic charges of atoms in mefloquine drugs, MF13, MF14 and MF15

Atomic charges (CNDO/2)					
MF13		MF14		MF15	
N1	5.1828	N1	5.1858	N1	5.1899
C2	3.8680	C2	3.8673	C2	3.8639
C3	4.0602	C3	4.0617	C3	4.0634
C4	3.9550	C4	3.9557	C4	3.9538
C5	3.9729	C5	3.9733	C5	3.9725
C6	4.0219	C6	4.0236	C6	4.0239
C7	3.9418	C7	3.9426	C7	3.9419
C8	4.0967	C8	4.0980	C8	4.0988
C9	3.8707	C9	3.8712	C9	3.8702
C10	3.9933	C10	3.9945	C10	3.9952
C11	3.9938	C11	4.0034	C11	4.0222
H12	0.9876	H12	0.9886	H12	0.9889
H13	0.9964	H13	0.9976	H13	0.9971
H14	1.0054	H14	1.0069	H14	1.0065
C15	3.8661	C15	3.8665	C15	3.8668
O16	6.2675	O16	6.2685	O16	6.2684
H17	0.8575	H17	0.8588	H17	0.8582
H18	1.0152	H18	1.0163	H18	1.0158
C19	3.9236	C19	3.9239	C19	3.9237
H20	1.0115	H20	1.0117	H20	1.0123
N2	5.1819	N21	5.1826	N21	5.1825
H22	0.9340	H22	0.9346	H22	0.9347
C23	3.9021	C23	3.9018	C23	3.9018
H24	1.0184	H24	1.0198	H24	1.0194
H25	1.0224	H25	1.0239	H25	1.0239
C26	3.9953	C26	3.9961	C26	3.9962
H27	0.9973	H27	0.9982	H27	0.9980
H28	1.0052	H28	1.0062	H28	1.0057
C29	3.9818	C29	3.9825	C29	3.9825
H30	1.0033	H30	1.0038	H30	1.0038
H31	1.0134	H31	1.0144	H31	1.0140
C32	3.9907	C32	3.9912	C32	3.9913
H33	1.0001	H33	1.0008	H33	1.0006
H34	0.9966	H34	0.9973	H34	0.9974
C35	3.9973	C35	3.9927	C35	3.9716
C36	3.9940	C36	4.0114	H36	4.0571
C37	3.9893	C37	3.9549	H37	3.8012
C38	3.9937	C38	4.0109	H38	4.0636
C39	3.9921	C39	3.9877	C39	3.9665
H40	0.9901	H40	0.9913	H40	0.9885
H41	1.0031	H41	1.0044	H41	0.9724
H42	1.0043	H42	1.0072	H42	0.9879
H43	1.0055	H43	1.0079	H43	1.0036
H44	1.0067	H44	0.9969	H44	0.9963
H45	0.9954	C45	3.3945	C45	3.3945
C46	3.3940	F46	7.2223	F46	7.2237
F47	7.2210	F47	7.2235	F47	7.2233
F48	7.2216	F48	7.2238	F48	7.2237
F49	7.2219				

Table 3.10f Atomic charges of atoms in mefloquine drugs, MF16, MF17 and MF18

Atomic charges (CNDO/2)					
MF16		MF17		MF18	
N1	5.1810	N1	5.1879	N1	5.1817
C2	3.8704	C2	3.8798	C2	3.8829
C3	4.0607	C3	4.0579	C3	4.0556
C4	3.9546	C4	3.9662	C4	3.9652
C5	3.9738	C5	4.0130	C5	4.0058
C6	4.0210	C6	3.9775	C6	4.0060
C7	3.9428	C7	3.9835	C7	3.9858
C8	4.0958	C8	4.0324	C8	3.9947
C9	3.8720	C9	3.9002	C9	3.9082
C10	3.9926	C10	3.9839	C10	3.9823
C11	3.9861	C11	4.0188	C11	3.9919
H12	0.9880	H12	0.9940	H12	0.9922
H13	0.9962	H13	1.0035	H13	1.0028
H14	1.0053	H14	1.0173	H14	1.0162
C15	3.8667	C15	3.8645	C15	3.8642
O16	6.2684	O16	6.2686	O16	6.2675
H17	0.8577	H17	0.8621	H17	0.8608
H18	1.0154	H18	1.0184	H18	1.0171
C19	3.9236	C19	3.9246	C19	3.9241
H20	1.0130	H20	1.0115	H20	1.0114
N2	5.1823	N21	5.1830	N21	5.1823
H22	0.9347	H22	0.9350	H22	0.9344
C23	3.9018	C23	3.9018	C23	3.9022
H24	1.0191	H24	1.0211	H24	1.0198
H25	1.0241	H25	1.0245	H25	1.0230
C26	3.9962	C26	3.9959	C26	3.9953
H27	0.9978	H27	0.9988	H27	0.9979
H28	1.0054	H28	1.0074	H28	1.0066
C29	3.9825	C29	3.9825	C29	3.9819
H30	1.0040	H30	1.0043	H30	1.0039
H31	1.0136	H31	1.0156	H31	1.0147
C32	3.9913	C32	3.9910	C32	3.9905
H33	1.0004	H33	1.0013	H33	1.0006
H34	0.9973	H34	0.9976	H34	0.9970
C35	3.9991	C35	3.9794	C35	4.0000
C36	3.9861	C36	4.0510	C36	3.9929
C37	3.9141	C37	3.8121	C37	3.9930
C38	3.9857	C38	4.0616	C38	3.9937
C39	3.9940	C39	3.9741	C39	3.9948
H40	0.9836	H40	1.0006	H40	1.0006
H41	0.9879	H41	0.9953	H41	1.0059
H42	0.9901	H42	0.9932	H42	1.0056
H43	0.9999	H43	1.0043	H43	1.0065
H44	0.9954	C44	4.0228	H44	1.0059
C45	3.3943	H45	0.9987	H45	1.0043
F46	7.2228	H46	0.9910	C46	4.0208
F47	7.2223	H47	0.9910	H47	0.9933
F48	7.2227	H48	0.9923	H48	0.9912
Cl49	7.1667			H49	0.9916

Table 3.10g Atomic charges of atoms in mefloquine drugs, MF19, MF20 and MF21

Atomic charges (CNDO/2)					
MF19		MF20		MF21	
N1	5.1835	N1	5.1788	N1	5.1848
C2	3.8816	C2	3.8848	C2	3.8811
C3	4.0562	C3	4.0551	C3	4.0578
C4	3.9649	C4	3.9638	C4	3.9641
C5	4.0054	C5	4.0060	C5	4.0057
C6	4.0067	C6	4.0040	C6	4.0070
C7	3.9854	C7	3.9858	C7	3.9861
C8	3.9953	C8	3.9930	C8	3.9956
C9	3.9079	C9	3.9087	C9	3.9083
C10	3.9828	C10	3.9808	C10	3.9833
C11	4.0006	C11	3.9833	C11	4.0088
H12	0.9925	H12	0.9919	H12	0.9935
H13	1.0030	H13	1.0016	H13	1.0031
H14	1.0164	H14	1.0149	H14	1.0166
C15	3.8641	C15	3.8644	C15	3.8650
O16	6.2673	O16	6.2671	O16	6.2682
H17	0.8609	H17	0.8598	H17	0.8611
H18	1.0171	H18	1.0163	H18	1.0174
C19	3.9243	C19	3.9238	C19	3.9244
H20	1.0112	H20	1.0126	H20	1.0126
N2	5.1824	N21	5.1820	N21	5.1827
H22	0.9343	H22	0.9344	H22	0.9350
C23	3.9020	C23	3.9021	C23	3.9018
H24	1.0199	H24	1.0191	H24	1.0206
H25	1.0230	H25	1.0231	H25	1.0248
C26	3.9951	C26	3.9953	C26	3.9960
H27	0.9979	H27	0.9975	H27	0.9984
H28	1.0067	H28	1.0059	H28	1.0070
C29	3.9818	C29	3.9818	C29	3.9825
H30	1.0039	H30	1.0040	H30	1.0046
H31	1.0148	H31	1.0140	H31	1.0151
C32	3.9905	C32	3.9905	C32	3.9912
H33	1.0005	H33	1.0001	H33	1.0008
H34	0.9969	H34	0.9970	H34	0.9976
C35	3.9944	C35	4.0008	C35	3.9814
C36	4.0092	C36	3.9840	C36	4.0488
C37	3.9576	C37	3.9158	C37	3.7706
C38	4.0098	C38	3.9848	C38	4.0494
C39	3.9896	C39	3.9959	C39	3.9764
H40	1.0012	H40	0.9935	H40	0.9950
H41	1.0061	H41	0.9895	H41	0.9834
H42	1.0073	H42	0.9902	H42	0.9838
H43	1.0066	H43	0.9986	H43	1.0000
H44	1.0045	H44	1.0030	H44	1.0047
C45	4.0204	C45	4.0211	C45	4.0207
H46	0.9933	H46	0.9937	H46	0.9945
H47	0.9914	H47	0.9900	H47	0.9917
H48	0.9918	H48	0.9904	H48	0.9921
C49	4.0857	C149	7.1682	F49	7.2053

Table 3.11 Dipole moments and total energies of chloroquine compounds

Compound no.	CNDO/2		ab initio	
	dipole moment (debye)	total energy (A.U.)	dipole moment (debye)	total energy (A.U.)
CQ1	6.277	-199.0030	4.926	-1144.2546
CQ2	5.957	-210.565	-	-
CQ3	6.346	-273.193	-	-
CQ4	5.273	-210.747	5.107	-794.0236
CQ5	4.601	-192.263	4.203	-730.4805
CQ6	4.690	-183.588	4.476	-697.2976
CQ7	4.194	-198.991	4.139	-1144.2446
CQ8	7.189	-198.316	4.639	-1144.2476
CQ9	2.602	-199.007	4.103	-1144.2156
CQ10	6.121	-207.677	4.831	-1177.4253
CQ11	6.528	-207.731	-	-
CQ12	6.294	-207.678	4.604	-1177.4228
CQ13	5.992	-211.426	4.082	-1191.0302
CQ14	5.032	-206.349	3.881	-1176.3862
CQ15	5.268	-241.013	-	-
CQ16	5.046	-189.022	3.955	-1143.2371
CQ17	6.518	-197.595	4.333	-1176.3255
CQ18	6.107	-173.118	5.094	-1111.1082
CQ19	6.308	-181.790	6.213	-1070.4639
CQ20	6.997	-181.312	1.593	-1570.6897
CQ21	8.168	-218.153	5.674	-1207.8164
CQ22	8.094	-250.628	-	-

Table 3.12 Dipole moments and total energies of mefloquine compounds

Compound no.	CNDO/2	
	dipole moment (debye)	total energy (A.U.)
MF1	6.130	-341.5520
MF2	4.323	-368.6401
MF3	5.274	-341.5618
MF4	3.615	-341.5645
MF5	2.239	-279.0337
MF6	3.727	-260.6199
MF7	3.289	-260.6140
MF8	3.378	-269.2942
MF9	3.371	-267.3528
MF10	2.906	-234.4678
MF11	1.698	-252.3706
MF12	3.316	-241.1949
MF13	2.957	-252.7549
MF14	5.489	-297.5991
MF15	5.611	-306.7477
MF16	4.627	-324.7568
MF17	6.084	-313.4734
MF18	1.743	-244.1661
MF19	3.012	-216.6600
MF20	3.212	-226.3248
MF21	3.149	-232.0629