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DFT-Based Prediction of Bioconcentration Factors of Polychlorinated Biphenyls in Fish Species Using Atomic Descriptors

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Atomic charge and density calculated by DFT method at twelve sites of biphenyl skeleton of polychlorinated biphenyls has been used to predict their bioconcentration factors. For prediction of bioconcentration factor, the 3D modeling and geometry optimization of all the compounds have been performed on workspace program of CAChe pro software of Fujitsu using the B88-PW91 GGA energy function with the DZVP basis set. Bioconcentration factor model, derived from partial atomic charges ($r^2 = 0.917$, $r^2_{CV} = 0.879$, $s = 0.270$) has better predicting power than the model derived from HOMO densities ($r^2 = 0.902$, $r^2_{CV} = 0.837$, $s = 0.307$) and can be used to predict bioconcentration factors of a large number of related compounds within limited time without any difficulty. One can also use these DFT-based atomic parameters in developing new methodology for chemical degradation of polychlorinated biphenyls.

Keywords: Atomic charge, Bioconcentration factor, DFT, HOMO Density, Polychlorinated biphenyls.

INTRODUCTION

Prediction of bioconcentration factors (BCFs) [1-4] of the polychlorinated biphenyls (PCBs) [5], a group of persistent organic pollutants [6-18] by QSAR modeling [19] using molecular descriptors were made time to time to increase the probability of success and reduce the time and cost in exploring the toxicological and ecological characteristics of molecules [20-35]. In this work, for the first time, we have used atomic descriptors: partial atom charges and HOMO densities [36] at various sites of polychlorinated biphenyls to predict their bioconcentration factors. Our interest in DFT-based prediction of bioconcentration factors using atomic descriptors was stimulated by the fact that DFT methods [37-39] are capable of generating a variety of local reactivity descriptors quite accurately.

EXPERIMENTAL

Fifty seven polychlorinated biphenyl congeners, listed in Table-1, are the study materials for the present study. These congeners have been taken from the literature with their experimental logarithmic bioconcentration factor values (log BCF_{exp}) for several fish species [24]. For BCF prediction, the 3D modeling [40] and geometry optimization of all the compounds have been performed on workspace program of CAChe pro software of Fujitsu using the B88-PW91 GGA energy function with the DZVP basis set [41]. The values of descriptors, partial atom charges and HOMO densities at 12 sites of polychlorinated biphenyls, have directly been obtained from DFT calculation results. The Project Leader program associated with CAChe has been used for multiple linear regression (MLR) analysis [42] and various regression equations have been developed for prediction of bioconcentration factor (log BCF_{pre}).

RESULTS AND DISCUSSION

The general chemical structure of polychlorinated biphenyls [5] is based upon the biphenyl's skeleton, containing one to ten atoms of chlorine and has 12 sites *viz.* 1, 2, 3, 4, 5, 6, 1', 2', 3', 4', 5' and 6'(Fig. 1). Biphenyl is well known aromatic compound and like other aromatic compounds its characteristic reaction is also electrophilic substitution reactions. Biphenyl, on chlorination (Fe/Cl_2) forms 4-chlorobiphenyl ($\Delta H_{Reaction}$ = -28.865 kcal/mol, $\Delta G_{Reaction}$ = -27.61 kcal/mol and $\Delta S_{Reaction}$ = -6.839 cal/mol K) as major product with some 2-chlorobiphenyl ($\Delta H_{Reaction}$ = -21.335 kcal/mol, $\Delta G_{Reaction}$ = -20.08 kcal/mol and $\Delta S_{Reaction}$ = -5.529 cal/mol K) as minor product. These on further chlorination give 4,4′-dichlorobiphenyl ($\Delta H_{Reaction}$ = -28.238 kcal/mol, $\Delta G_{Reaction}$ = -25.728 kcal/mol and $\Delta S_{Reaction}$ = -9.741 cal/mol K) as major product and some 2,4′-dichlorobiphenyl ($\Delta H_{Reaction}$ = -21.335 kcal/mol, $\Delta G_{Reaction}$ =

TABLE-1
BIPHENYL, ITS CHLORO-DERIVATIVES AND THEIR CONGENERS WITH THEIR EXPERIMENTAL LOGARITHMIC BCF

S. No.	Chemical Name	[a]log BCF_{exp}	S. No.	Chemical Name	[a]log BCF_{exp}
1	Biphenyl	2.64	30	2,3,3`,4,4`-pentachloro-	5.00
2	4-chloro-	2.77	31	2,3,3`,4,6-pentachloro-	5.00
3	2,2`-dichloro-	3.38	32	2,3`,4,4`,5-pentachloro-	5.00
4	2,3-dichloro-	4.11	33	3,3`,4,4`,5-pentachloro-	5.81
5	2,3`-dichloro-	3.80	34	2,2`,3,3`,4,4`-hexachloro-	5.77
6	2,4-dichloro-	3.55	35	2,2`3,3`,6,6`-hexachloro-	5.43
7	2,4`-dichloro-	3.57	36	2,2`,3,4,4`,5-hexachloro-	5.88
8	2,5-dichloro-	3.89	37	2,2`3,4,4`,5`-hexachloro-	5.39
9	3,5-dichloro-	3.78	38	2,2`,3,4,5,5`-hexachloro-	5.81
10	4,4`-dichloro-	3.28	39	2,2`,3,4`,5,6`-hexachloro-	5.39
11	2,2`,5-trichloro-	4.11	40	2,2`,3,5,5`,6-hexachloro-	5.54
12	2,4,4`-trichloro-	4.20	41	2,2`,4,4`,5,5`-hexachloro-	5.65
13	2,4,5-trichloro-	4.26	42	2,2`,4,4`,6,6`-hexachloro-	4.93
14	2,4`,5-trichloro-	4.23	43	2,3,3`,4,4`,5-hexachloro-	5.39
15	2,2`,3,3`-tetrachloro-	4.23	44	2,3,3`,4,4`,5`-hexachloro-	5.39
16	2,2`,3,5`-tetrachloro-	4.84	45	3,3`,4,4`,5,5`-hexachloro-	5.97
17	2,2`,4,4`-tetrachloro-	4.85	46	2,2`,3,3`,4,5,6`-heptachloro-	5.80
18	2,2`,4,5-tetrachloro-	5.00	47	2,2`,3,4,4`,5,5`-heptachloro-	5.80
19	2,2`,4,5`-tetrachloro-	4.84	48	2,2`,3,4,4`,5,6`-heptachloro-	5.80
20	2,2`,5,5`-tetrachloro-	4.63	49	2,2`,3,4,4`,5`,6-heptachloro-	5.84
21	2,2`,6,6`-tetrachloro-	3.85	50	2,2`,3,4`,5,5`,6-heptachloro-	5.80
22	2,3,4`,6-tetrachloro-	4.60	51	2,3,3`,4,4`,5`,6-heptachloro-	5.84
23	2,3`,4`,5-tetrachloro-	4.77	52	2,2`,3,3`,4,4`5,5`-octachloro-	5.81
24	3,3`,4,4`-tetrachloro-	4.59	53	2,2`,3,3`,4,4`5,6-octachloro-	5.92
25	2,2`,3,4,5`-pentachloro-	5.38	54	2,2`,3,3`,4,4`5,6`-octachloro-	5.92
26	2,2`,3,4`,5-pentachloro-	5.00	55	2,2`,3,3`,4, 5,5`,6-octachloro-	5.88
27	2,2`,3`,4,5`-pentachloro-	5.43	56	2,2`,3,3`,5,5`,6,6`-octachloro-	5.82
28	2,2`,4,4`,5-pentachloro-	5.00	57	2,2`,3,3`,4,5,5`,6,6`-nonachloro-	5.71
29	2,2`,4,5,5`-pentachloro-	5.40	58	Decachloro-	5.44

[a]Experimental logarithmic BCF values as taken from literature [Ref. 24]

-19.453 kcal/mol and $\Delta S_{Reaction}$ = -6.954 cal/mol K) and 2,2′-dichlorobiphenyl ($\Delta H_{Reaction}$ = -6.275 kcal/mol, $\Delta G_{Reaction}$ = -3.765 kcal/mol and $\Delta S_{Reaction}$ = -8.978 cal/mol K), respectively [43]. The vibrational frequency calculations were performed to determine the above thermodynamic quantities at 298K by DFT method. Actually in biphenyl the presence of one phenyl ring is found to activate the other for electrophilic substitution and directs the new group to *o*- and *p*-positions. In monosubstituted biphenyl, the substituent invariably enters the unsubstituted ring (in *o*- and *p*-positions) whether the substituent already present is activating or deactivating. In order to predict the electrophilic sites of attack, most negative charged sites (Q_{min}) and/or orbital of high electron density (HOMO) must be known [44,45]. The partial atomic charges and HOMO densities of all the twelve sites have been evaluated by DFT method and are reported in Tables 2 and 3, respectively.

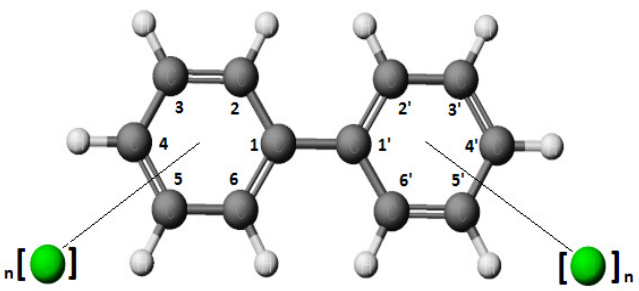

Fig. 1

To correlate the effect of the number and position of chlorine atoms on atomic charges and HOMO densities at these sites and finally their effect on the bioconcentration factors, QSAR models have been developed. For sake of simplicity, the study has been divided into following sub-headings:

Partial atomic charge (Q): The charge distributions (Q) of each atom [44] of all the polychlorinated biphenyls were calculated by DFT method and the results are reported in Table-2. A reference to this table shows that all the compounds bear positive charges on sites 1 and 1' indicating that the rest sites are suitable for the attack of Cl^+ ion (an electrophile) for substitution reaction. MLR analyses [42] were employed to develop reliable QSAR model for the prediction of bioconcentration factor. For MLR analysis, partial atomic charges of 12 sites (Table-2) were used as independent variables and the experimental logarithmic bioconcentration factor values as dependent variable. MLR analysis has been made by Project Leader software associated with CAChe, using these charges in various combinations. The best twelve models for k = 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 (eqns. 1-12) are selected on the basis of correlation coefficient (r^2) and cross-validated correlation coefficient (r^2_{cv}) and are presented below:

$$\log BCF_{pre} = 7.31267 \times Q3 + 5.86732 \quad (1)$$

$$\log BCF_{pre} = 3.98933 \times Q4 + 6.78289 \times Q3 + 6.25715 \quad (2)$$

$$\log BCF_{pre} = 2.73959 \times Q5 + 3.83783 \times Q4 + 5.75907 \times Q3 + 6.48859 \quad (3)$$

TABLE-2
ATOMIC CHARGES AT VARIOUS SITES OF BIPHENYL AND ITS DERIVATIVES AS CALCULATED BY DFT METHODS, EXPERIMENTAL BCF AND PREDICTED BCF

S. No.	[b]Q												[c]log BCF_{exp}	[d]log BCF_{pre}
	Q_6	Q_5	Q_4	Q_3	Q_2	Q_1	$Q_{1'}$	$Q_{2'}$	$Q_{3'}$	$Q_{4'}$	$Q_{5'}$	$Q_{6'}$		
1	-0.316	-0.242	-0.239	-0.241	-0.316	0.254	0.254	-0.316	-0.242	-0.239	-0.241	-0.316	2.64	2.52
2	-0.310	-0.231	-0.080	-0.230	-0.312	0.279	0.253	-0.314	-0.240	-0.239	-0.240	-0.314	2.77	3.05
3	-0.258	-0.284	-0.240	-0.227	-0.162	0.304	0.304	-0.164	-0.228	-0.240	-0.283	-0.257	3.38	3.41
4	-0.312	-0.255	-0.235	-0.078	-0.150	0.338	0.258	-0.287	-0.246	-0.236	-0.252	-0.298	4.11	3.90
5[a]	-0.285	-0.263	-0.233	-0.238	-0.176	0.314	0.296	-0.255	-0.092	-0.243	-0.235	-0.326	3.80	3.49
6	-0.288	-0.253	-0.084	-0.217	-0.176	0.337	0.261	-0.293	-0.242	-0.238	-0.248	-0.307	3.55	3.70
7	-0.292	-0.261	-0.236	-0.233	-0.177	0.315	0.286	-0.287	-0.234	-0.081	-0.238	-0.301	3.57	3.61
8	-0.244	-0.120	-0.245	-0.215	-0.204	0.350	0.259	-0.288	-0.243	-0.235	-0.252	-0.304	3.89	3.79
9	-0.300	-0.074	-0.242	-0.077	-0.298	0.307	0.246	-0.301	-0.246	-0.231	-0.244	-0.306	3.78	3.96
10	-0.309	-0.230	-0.081	-0.229	-0.310	0.277	0.277	-0.309	-0.230	-0.081	-0.229	-0.310	3.28	3.50
11	-0.252	-0.072	-0.216	-0.209	-0.184	0.227	0.209	-0.167	-0.229	-0.219	-0.234	-0.267	4.11	4.29
12	-0.285	-0.252	-0.085	-0.217	-0.176	0.337	0.287	-0.288	-0.234	-0.081	-0.238	-0.301	4.20	4.14
13	-0.257	-0.099	-0.093	-0.214	-0.211	0.380	0.252	-0.287	-0.242	-0.235	-0.250	-0.303	4.26	4.11
14	-0.244	-0.119	-0.244	-0.215	-0.204	0.349	0.282	-0.281	-0.235	-0.079	-0.240	-0.298	4.23	4.21
15	-0.285	-0.222	-0.227	-0.073	-0.137	0.219	0.220	-0.143	-0.071	-0.229	-0.222	-0.279	4.23	4.52
16	-0.252	-0.219	-0.228	-0.069	-0.131	0.205	0.276	-0.143	-0.243	-0.207	-0.246	-0.154	4.84	4.61
17	-0.291	-0.235	-0.027	-0.233	-0.139	0.238	0.239	-0.139	-0.233	-0.027	-0.235	-0.291	4.85	4.68
18	-0.310	-0.036	-0.039	-0.221	-0.166	0.268	0.238	-0.158	-0.231	-0.206	-0.222	-0.302	5.00	4.94
19[a]	-0.281	-0.236	-0.026	-0.234	-0.136	0.230	0.264	-0.178	-0.207	-0.224	-0.033	-0.305	4.84	4.64
20	-0.305	-0.034	-0.223	-0.206	-0.179	0.267	0.267	-0.179	-0.207	-0.223	-0.035	-0.305	4.63	4.64
21	-0.111	-0.252	-0.185	-0.251	-0.111	0.255	0.255	-0.111	-0.252	-0.185	-0.252	-0.111	3.85	4.06
22	-0.189	-0.234	-0.219	-0.067	-0.161	0.322	0.194	-0.292	-0.214	-0.038	-0.214	-0.291	4.60	4.65
23[a]	-0.265	-0.068	-0.250	-0.218	-0.183	0.325	0.313	-0.286	-0.047	-0.058	-0.235	-0.334	4.77	4.90
24	-0.330	-0.227	-0.062	-0.044	-0.305	0.296	0.296	-0.305	-0.044	-0.062	-0.227	-0.330	4.59	4.58
25	-0.316	-0.228	-0.053	-0.042	-0.152	0.265	0.268	-0.178	-0.206	-0.224	-0.032	-0.310	5.38	5.17
26	-0.320	-0.015	-0.247	-0.016	-0.186	0.281	0.223	-0.137	-0.233	-0.024	-0.240	-0.269	5.00	5.35
27	-0.307	-0.040	-0.035	-0.223	-0.162	0.263	0.260	-0.157	-0.047	-0.231	-0.206	-0.319	5.43	5.17
28[a]	-0.310	-0.037	-0.038	-0.221	-0.167	0.269	0.236	-0.140	-0.234	-0.024	-0.236	-0.286	5.00	5.23
29	-0.266	-0.037	-0.038	-0.216	-0.172	0.240	0.217	-0.147	-0.229	-0.028	-0.230	-0.252	5.40	5.29
30	-0.309	-0.256	-0.052	-0.064	-0.150	0.341	0.305	-0.288	-0.045	-0.062	-0.236	-0.321	5.00	5.23
31	-0.168	-0.262	-0.030	-0.080	-0.146	0.310	0.207	-0.297	-0.017	-0.239	-0.186	-0.312	5.00	5.06
32	-0.326	-0.040	-0.039	-0.227	-0.210	0.306	0.245	-0.319	-0.020	-0.056	-0.203	-0.350	5.00	5.02
33[a]	-0.345	-0.024	-0.091	-0.027	-0.345	0.338	0.276	-0.291	-0.048	-0.056	-0.233	-0.321	5.81	4.93
34	-0.317	-0.227	-0.052	-0.043	-0.148	0.262	0.261	-0.149	-0.044	-0.052	-0.227	-0.316	5.77	5.50
35	-0.138	-0.232	-0.213	-0.066	-0.107	0.279	0.279	-0.108	-0.067	-0.213	-0.231	-0.137	5.43	4.99
36	-0.329	-0.027	-0.068	-0.020	-0.186	0.283	0.222	-0.136	-0.234	-0.025	-0.237	-0.269	5.88	5.76
37	-0.280	-0.230	-0.053	-0.045	-0.146	0.236	0.235	-0.159	-0.223	-0.035	-0.040	-0.273	5.39	5.51
38[a]	-0.339	-0.028	-0.068	-0.015	-0.194	0.296	0.261	-0.179	-0.205	-0.222	-0.036	-0.298	5.81	5.65
39	-0.287	-0.011	-0.245	-0.017	-0.165	0.266	0.244	-0.104	-0.261	-0.006	-0.262	-0.111	5.39	5.29
40	-0.168	-0.042	-0.241	-0.042	-0.165	0.319	0.234	-0.157	-0.209	-0.217	-0.035	-0.251	5.54	5.45
41	-0.305	-0.042	-0.036	-0.221	-0.169	0.267	0.267	-0.169	-0.221	-0.036	-0.042	-0.304	5.65	5.51
42	-0.091	-0.259	-0.008	-0.260	-0.091	0.242	0.244	-0.091	-0.259	-0.007	-0.260	-0.092	4.93	4.98
43[a]	-0.370	-0.024	-0.070	-0.027	-0.240	0.348	0.241	-0.317	-0.020	-0.056	-0.204	-0.350	5.39	5.41
44	-0.303	-0.261	-0.049	-0.069	-0.140	0.331	0.352	-0.328	-0.030	-0.097	-0.032	-0.331	5.39	5.61
45	-0.330	-0.032	-0.089	-0.032	-0.330	0.318	0.318	-0.330	-0.032	-0.089	-0.032	-0.330	5.97	5.37
46	-0.287	-0.030	-0.065	-0.019	-0.167	0.259	0.288	-0.126	-0.071	-0.211	-0.233	-0.157	5.80	5.78
47	-0.298	-0.062	-0.068	-0.026	-0.189	0.265	0.239	-0.185	-0.195	-0.061	-0.065	-0.264	5.80	5.83
48[a]	-0.292	-0.023	-0.070	-0.016	-0.169	0.264	0.245	-0.106	-0.260	-0.006	-0.260	-0.110	5.80	5.73
49	-0.143	-0.260	-0.027	-0.077	-0.114	0.278	0.233	-0.145	-0.222	-0.035	-0.039	-0.253	5.84	5.83
50	-0.135	-0.260	-0.027	-0.079	-0.114	0.272	0.230	-0.128	-0.044	-0.053	-0.229	-0.257	5.80	5.80
51	-0.173	-0.260	-0.028	-0.081	-0.148	0.317	0.230	-0.323	0.002	-0.073	0.002	-0.325	5.84	5.59
52	-0.343	-0.026	-0.067	-0.020	-0.191	0.297	0.297	-0.191	-0.020	-0.067	-0.026	-0.342	5.81	6.33
53[a]	-0.170	-0.061	-0.055	-0.062	-0.163	0.318	0.223	-0.126	-0.044	-0.055	-0.228	-0.253	5.92	6.07
54	-0.293	-0.023	-0.069	-0.017	-0.170	0.264	0.278	-0.113	-0.076	-0.029	-0.258	-0.144	5.92	6.01
55	-0.184	-0.067	-0.052	-0.063	-0.160	0.330	0.262	-0.167	-0.020	-0.242	-0.015	-0.285	5.88	6.01
56	-0.146	-0.042	-0.241	-0.041	-0.146	0.311	0.311	-0.147	-0.042	-0.241	-0.041	-0.146	5.82	5.74
57	-0.148	-0.061	-0.057	-0.061	-0.146	0.308	0.311	-0.148	-0.041	-0.241	-0.040	-0.148	5.71	6.12
58[a]	-0.155	-0.057	-0.059	-0.057	-0.152	0.314	0.315	-0.157	-0.058	-0.058	-0.060	-0.148	5.44	6.43

[a]Data point not used in the model, [b]Q is partial atomic charge of the carbon atom at a respective site of the molecule, [c]Experimental logarithmic BCF values as taken from literature [24], [d]Predicted logarithmic BCF values by eqn. 7.

TABLE-3
HOMO DENSITIES AT VARIOUS SITES OF BIPHENYL AND ITS DERIVATIVES AS CALCULATED BY DFT METHODS, EXPERIMENTAL BCF AND PREDICTED BCF

S. No.	[b]ρ_H												[c]log BCF_{exp}	[d]log BCF_{pre}
	ρ_{6H}	ρ_{5H}	ρ_{4H}	ρ_{3H}	ρ_{2H}	ρ_{1H}	$\rho_{1'H}$	$\rho_{2'H}$	$\rho_{3'H}$	$\rho_{4'H}$	$\rho_{5'H}$	$\rho_{6'H}$		
1	0.082	0.024	0.164	0.024	0.082	0.124	0.124	0.082	0.024	0.164	0.024	0.082	2.64	2.92
2	0.068	0.032	0.142	0.033	0.068	0.125	0.103	0.073	0.020	0.143	0.019	0.074	2.77	3.54
3	0.012	0.063	0.080	0.005	0.116	0.105	0.104	0.115	0.004	0.080	0.062	0.012	3.38	3.48
4	0.096	0.011	0.145	0.024	0.049	0.098	0.141	0.069	0.038	0.171	0.020	0.088	4.11	3.70
5	0.043	0.024	0.109	0.009	0.079	0.099	0.102	0.015	0.070	0.174	0.005	0.159	3.80	4.04
6	0.053	0.033	0.118	0.021	0.074	0.114	0.120	0.070	0.028	0.154	0.020	0.079	3.55	3.41
7	0.050	0.022	0.111	0.009	0.081	0.087	0.137	0.061	0.043	0.145	0.034	0.067	3.57	3.96
8	0.014	0.054	0.127	0.004	0.141	0.093	0.116	0.065	0.027	0.145	0.022	0.070	3.89	3.39
9	0.074	0.019	0.171	0.018	0.077	0.091	0.140	0.079	0.028	0.172	0.029	0.077	3.78	3.72
10[a]	0.062	0.028	0.126	0.028	0.062	0.106	0.106	0.062	0.028	0.126	0.028	0.062	3.28	4.34
11[a]	0.047	0.173	0.068	0.054	0.183	0.070	0.013	0.010	0.000	0.009	0.006	0.002	4.11	5.06
12	0.049	0.026	0.102	0.018	0.065	0.091	0.123	0.059	0.038	0.134	0.031	0.063	4.20	4.31
13	0.028	0.047	0.120	0.009	0.098	0.102	0.112	0.066	0.026	0.143	0.020	0.071	4.26	3.83
14	0.021	0.035	0.111	0.003	0.112	0.073	0.127	0.055	0.040	0.133	0.035	0.058	4.23	4.32
15	0.068	0.062	0.005	0.082	0.072	0.003	0.003	0.089	0.100	0.006	0.076	0.084	4.23	4.32
16	0.152	0.129	0.012	0.175	0.154	0.005	0.001	0.004	0.008	0.000	0.008	0.005	4.84	4.65
17	0.017	0.069	0.088	0.007	0.064	0.119	0.119	0.064	0.008	0.089	0.069	0.018	4.85	4.70
18	0.006	0.134	0.098	0.006	0.129	0.109	0.051	0.048	0.002	0.041	0.033	0.006	5.00	5.03
19	0.008	0.017	0.030	0.005	0.019	0.038	0.073	0.172	0.040	0.073	0.149	0.029	4.84	4.97
20	0.011	0.085	0.054	0.018	0.110	0.052	0.051	0.107	0.017	0.053	0.082	0.011	4.63	4.84
21	0.065	0.112	0.003	0.112	0.065	0.002	0.001	0.062	0.106	0.003	0.106	0.062	3.85	3.88
22	0.061	0.002	0.054	0.025	0.008	0.049	0.182	0.047	0.058	0.154	0.057	0.047	4.60	4.95
23	0.015	0.036	0.102	0.003	0.106	0.071	0.105	0.025	0.057	0.139	0.017	0.086	4.77	4.79
24[a]	0.076	0.017	0.127	0.038	0.037	0.092	0.092	0.037	0.038	0.127	0.017	0.076	4.59	5.36
25	0.017	0.007	0.031	0.011	0.008	0.029	0.073	0.174	0.041	0.072	0.151	0.030	5.38	5.26
26	0.073	0.141	0.027	0.074	0.187	0.040	0.022	0.009	0.003	0.016	0.009	0.004	5.00	5.09
27	0.011	0.159	0.100	0.010	0.143	0.113	0.026	0.008	0.007	0.031	0.004	0.022	5.43	5.48
28	0.004	0.116	0.093	0.004	0.115	0.101	0.073	0.037	0.007	0.055	0.037	0.013	5.00	5.39
29	0.020	0.169	0.095	0.012	0.146	0.106	0.021	0.009	0.002	0.013	0.009	0.004	5.40	5.74
30	0.059	0.016	0.102	0.024	0.040	0.081	0.103	0.026	0.056	0.138	0.014	0.089	5.00	5.30
31	0.038	0.001	0.033	0.031	0.002	0.038	0.071	0.026	0.145	0.117	0.017	0.199	5.00	4.82
32	0.007	0.067	0.086	0.002	0.085	0.082	0.098	0.019	0.044	0.114	0.022	0.061	5.00	5.34
33	0.056	0.022	0.125	0.026	0.050	0.080	0.099	0.034	0.042	0.131	0.019	0.076	5.81	5.51
34	0.033	0.048	0.102	0.019	0.036	0.115	0.115	0.036	0.019	0.102	0.048	0.033	5.77	5.48
35	0.079	0.057	0.014	0.100	0.048	0.009	0.008	0.045	0.092	0.013	0.053	0.073	5.43	5.36
36	0.012	0.122	0.067	0.011	0.126	0.082	0.071	0.033	0.005	0.050	0.042	0.008	5.88	5.50
37[a]	0.001	0.001	0.001	0.000	0.002	0.006	0.107	0.151	0.016	0.095	0.183	0.026	5.39	6.65
38	0.003	0.012	0.022	0.002	0.016	0.022	0.069	0.174	0.045	0.069	0.156	0.039	5.81	5.38
39	0.107	0.150	0.018	0.091	0.189	0.030	0.000	0.001	0.001	0.000	0.001	0.001	5.39	5.32
40	0.005	0.005	0.000	0.005	0.006	0.001	0.064	0.176	0.056	0.062	0.173	0.060	5.54	5.70
41	0.003	0.079	0.072	0.002	0.082	0.078	0.077	0.081	0.002	0.071	0.078	0.003	5.65	5.71
42	0.027	0.029	0.077	0.039	0.022	0.141	0.142	0.023	0.037	0.078	0.031	0.027	4.93	4.62
43	0.011	0.049	0.082	0.003	0.067	0.072	0.112	0.018	0.052	0.129	0.026	0.067	5.39	5.50
44	0.060	0.019	0.108	0.028	0.038	0.090	0.093	0.041	0.039	0.137	0.021	0.065	5.39	5.28
45	0.051	0.027	0.130	0.027	0.051	0.086	0.086	0.051	0.027	0.130	0.027	0.051	5.97	5.50
46	0.039	0.107	0.027	0.028	0.106	0.039	0.007	0.039	0.073	0.010	0.043	0.058	5.80	5.45
47	0.002	0.038	0.044	0.001	0.044	0.048	0.097	0.114	0.005	0.088	0.125	0.007	5.80	6.11
48	0.063	0.174	0.046	0.043	0.176	0.066	0.001	0.002	0.001	0.000	0.002	0.001	5.80	5.64
49[a]	0.001	0.001	0.001	0.000	0.002	0.005	0.108	0.149	0.015	0.095	0.182	0.027	5.84	6.73
50	0.140	0.047	0.055	0.191	0.052	0.049	0.003	0.007	0.010	0.001	0.006	0.008	5.80	5.97
51	0.052	0.003	0.057	0.040	0.005	0.067	0.121	0.033	0.045	0.148	0.043	0.034	5.84	5.66
52	0.004	0.081	0.062	0.003	0.086	0.069	0.069	0.084	0.003	0.062	0.079	0.003	5.81	5.83
53	0.125	0.127	0.004	0.128	0.125	0.003	0.000	0.005	0.009	0.001	0.004	0.007	5.92	6.07
54	0.061	0.172	0.048	0.040	0.175	0.067	0.002	0.003	0.001	0.000	0.002	0.001	5.92	5.69
55	0.001	0.004	0.001	0.001	0.004	0.001	0.030	0.187	0.088	0.018	0.147	0.105	5.88	5.56
56	0.067	0.068	0.002	0.068	0.067	0.002	0.002	0.067	0.068	0.002	0.068	0.067	5.82	6.00
57	0.009	0.010	0.000	0.010	0.009	0.000	0.003	0.126	0.124	0.003	0.124	0.126	5.71	6.06
58[a]	0.067	0.063	0.002	0.068	0.062	0.002	0.002	0.065	0.071	0.002	0.066	0.070	5.44	6.10

[a]Data point not used in the model, [b]ρ_H HOMO density of the carbon atom at a respective site of the molecule, [c]Experimental logarithmic BCF values as taken from literature [24], [d]Predicted logarithmic BCF values by eqn. 22.

$$\log BCF_{pre} = 3.68829 \times Q5 + 3.6534 \times Q4 + 5.20816 \times Q3 + 5.51755 \times Q2 + 7.52158 \quad (4)$$

$$\log BCF_{pre} = 3.58483 \times Q5 + 3.4302 \times Q4 + 4.6663 \times Q3 + 5.57053 \times Q2 + 1.44939 \times Q3' + 7.6443 \quad (5)$$

$$\log BCF_{pre} = 2.26451 \times Q6 + 4.02966 \times Q5 + 3.30571 \times Q4 + 4.93578 \times Q3 + 3.97865 \times Q2 + 1.29065 \times Q4' + 7.97909 \quad (6)$$

$$\log BCF_{pre} = 1.65056 \times Q6 + 3.82019 \times Q5 + 3.56547 \times Q4 + 4.6762 \times Q3 + 4.32587 \times Q2 + 0.425289 \times Q1 + 1.2721 \times Q5' + 7.7787 \quad (7)$$

$$\log BCF_{pre} = 4.37131 \times Q6 + 4.54443 \times Q5 + 3.85701 \times Q4 + 5.57252 \times Q3 + 4.65045 \times Q2 - 3.36609 \times Q1 + 5.8007 \times Q1' - 3.55156 \times Q6' + 7.21326 \quad (8)$$

$$\log BCF_{pre} = 4.38018 \times Q6 + 4.61634 \times Q5 + 3.86303 \times Q4 + 5.58354 \times Q3 + 4.82281 \times Q2 - 3.59199 \times Q1 + 5.81215 \times Q1' - 0.274077 \times Q2' - 3.46388 \times Q6' + 7.2887 \quad (9)$$

$$\log BCF_{pre} = 2.70639 \times Q5 + 2.36757 \times Q4 + 3.42427 \times Q3 + 3.69139 \times Q2 + 1.65867 \times Q1 + 0.706296 \times Q1' + 2.07852 \times Q2' + 1.86941 \times Q3' + 1.98578 \times Q4' + 1.96214 \times Q5' + 7.34506 \quad (10)$$

$$\log BCF_{pre} = 4.91357 \times Q6 + 4.57264 \times Q5 + 3.20577 \times Q4 + 5.33602 \times Q3 + 4.48698 \times Q2 - 3.71172 \times Q1 + 6.74472 \times Q1' + 0.0458702 \times Q2' + 0.121179 \times Q3' + 1.77042 \times Q4' - 3.88007 \times Q6' + 7.25792 \quad (11)$$

$$\log BCF_{pre} = 4.01452 \times Q6 + 4.19279 \times Q5 + 3.0018 \times Q4 + 4.85451 \times Q3 + 4.18059 \times Q2 - 2.61371 \times Q1 + 5.39416 \times Q1' + 0.421213 \times Q2' + 0.487842 \times Q3' + 1.86228 \times Q4' + 0.57685 \times Q5' - 2.95444 \times Q6' + 7.35851 \quad (12)$$

The regression summary of these equations has also been presented in Table-4. A close look at this table indicates that the reliable model is the eqn. 7 as it has highest value of 'r^2' and lowest value of 's' among the rest equations. All the descriptors of this model have positive coefficient values indicating that these have direct relationship with the bioconcentration factors, except Q_1 and $Q_{6'}$, which have a negative coefficient values indicating that these have inverse relationship with bioconcentration factors. Predicted bioconcentration factor as obtained by this equation has also been presented in Table-2. The predicted bioconcentration factor is reliable as it is evident from its standard error value (0.27).

TABLE-4
REGRESSION SUMMARY OF MODELS DERIVED FROM ATOMIC CHARGES AS INDEPENDENT VARIABLES

Eqn. No.	k	n	r^2	r^2_{CV}	s
1	1	49	0.645	0.639	0.482
2	2	49	0.814	0.793	0.355
3	3	49	0.878	0.869	0.292
4	4	56	0.900	0.874	0.288
5	5	56	0.910	0.886	0.275
6	6	56	0.914	0.887	0.273
7	7	56	0.917	0.879	0.270
8	8	57	0.908	0.845	0.288
9	9	57	0.909	0.843	0.291
10	10	57	0.911	0.832	0.292
11	11	58	0.914	0.839	0.288
12	12	58	0.916	0.834	0.288

HOMO density (ρHOMO = ρ_H): FMO theory predicts that the preferable electrophilic reaction in a molecule will take place at the site, where the relative density of the HOMO is high [45]. The HOMO density of each atom of all the polychlorinated biphenyls were calculated by DFT method and the result are reported in Table-3. Similar to partial atomic charges, MLR analysis [42] has also been made by same software using HOMO densities of 12 sites in various combinations. The best twelve models, for k = 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 (eqns. 13-24) are presented below:

$$\log BCF_{pre} = -11.0528 \times \rho_{4H} + 5.66552 \quad (13)$$

$$\log BCF_{pre} = -12.4484 \times \rho_{4H} - 5.57528 \times \rho_{3'H} + 5.96252 \quad (14)$$

$$\log BCF_{pre} = -16.0072 \times \rho_{4H} - 7.84311 \times \rho_{3H} - 6.61487 \times \rho_{2'H} + 6.65743 \quad (15)$$

$$\log BCF_{pre} = -9.90346 \times \rho_{6H} - 1.81391 \times \rho_{5H} - 14.4676 \times \rho_{4H} - 7.98262 \times \rho_{2'H} + 6.89501 \quad (16)$$

$$\log BCF_{pre} = -6.84855 \times \rho_{3H} - 8.00967 \times \rho_{2H} - 4.06683 \times \rho_{1H} - 10.6476 \times \rho_{1'H} - 9.67037 \times \rho_{6'H} + 7.27363 \quad (17)$$

$$\log BCF_{pre} = -18.5163 \times \rho_{3H} - 20.1669 \times \rho_{2H} - 16.1387 \times \rho_{1H} - 16.802 \times \rho_{1'H} - 17.9421 \times \rho_{2'H} - 22.4239 \times \rho_{3'H} + 11.264 \quad (18)$$

$$\log BCF_{pre} = -18.5657 \times \rho_{3H} - 19.515 \times \rho_{2H} - 14.6725 \times \rho_{1H} - 15.8494 \times \rho_{1'H} - 17.6719 \times \rho_{2'H} - 15.3895 \times \rho_{3'H} - 5.63894 \times \rho_{6'H} + 11.0543 \quad (19)$$

$$\log BCF_{pre} = -21.2936 \times \rho_{3H} - 22.650 \times \rho_{2H} - 20.9979 \times \rho_{1H} - 8.16519 \times \rho_{1'H} - 12.2259 \times \rho_{2'H} - 23.1899 \times \rho_{3'H} - 8.84995 \times \rho_{4'H} - 11.1331 \times \rho_{5'H} + 12.1834 \quad (20)$$

$$\log BCF_{pre} = -15.3068 \times \rho_{5H} - 3.07892 \times \rho_{4H} - 21.8963 \times \rho_{3H} - 11.4376 \times \rho_{2H} - 10.5214 \times \rho_{1H} - 22.539 \times \rho_{1'H} - 21.2722 \times \rho_{2'H} - 11.2643 \times \rho_{3'H} - 12.9504 \times \rho_{6'H} + 12.318 \quad (21)$$

$$\log BCF_{pre} = -5.77578 \times \rho_{6H} - 15.3989 \times \rho_{5H} - 1.76363 \times \rho_{4H} - 17.1514 \times \rho_{3H} - 11.205 \times \rho_{2H} - 11.8282 \times \rho_{1H} - 21.9404 \times \rho_{1'H} - 21.613 \times \rho_{2'H} - 12.7592 \times \rho_{3'H} - 11.5088 \times \rho_{6'H} + 12.3434 \quad (22)$$

$$\log BCF_{pre} = -12.7279 \times \rho_{6H} - 5.95064 \times \rho_{5H} + 3.019 \times \rho_{4H} - 13.0376 \times \rho_{3H} - 20.0458 \times \rho_{2H} - 24.851 \times \rho_{1H} - 8.06609 \times \rho_{1'H} - 12.8066 \times \rho_{2'H} - 25.1578 \times \rho_{3'H} - 10.5185 \times \rho_{4'H} - 14.2126 \times \rho_{5'H} + 13.0287 \quad (23)$$

$$\log BCF_{pre} = -11.2483 \times \rho_{6H} - 9.69523 \times \rho_{5H} + 0.806812 \times \rho_{4H} - 15.1178 \times \rho_{3H} - 17.7574 \times \rho_{2H} - 21.4003 \times \rho_{1H} - 13.8613 \times \rho_{1'H} - 12.9165 \times \rho_{2'H} - 17.2176 \times \rho_{3'H} - 5.65047 \times \rho_{4'H} - 14.4009 \times \rho_{5'H} - 8.67902 \times \rho_{6'H} + 13.2 \quad (24)$$

The regression summary of these equations has also been presented in Table-5, which indicates that the most reliable model is the eqn. 22 as it has highest value of 'r^2' and lowest value of 's' among the rest equations. All the descriptors of this model have negative coefficient values, indicating that these have inverse relationship with bioconcentration factors, except ρ_{4H}, which has a positive coefficient values indicating that it has a direct relationship with the bioconcentration factors. Predicted bioconcentration factor as obtained by this equation has also been presented in Table-3. The predicted

TABLE-5
REGRESSION SUMMARY OF MODELS DERIVED FROM HOMO DENSITIES AS INDEPENDENT VARIABLES

Eqn. No.	k	n	r^2	r^2_{CV}	s
13	1	48	0.638	0.614	0.532
14	2	48	0.763	0.747	0.443
15	3	48	0.825	0.811	0.386
16	4	48	0.826	0.807	0.389
17	5	48	0.830	0.797	0.385
18	6	50	0.825	0.754	0.396
19	7	48	0.832	0.775	0.396
20	8	48	0.867	0.802	0.335
21	9	53	0.865	0.749	0.346
22	10	52	0.902	0.837	0.307
23	11	56	0.865	0.765	0.353
24	12	58	0.840	0.693	0.397

bioconcentration factor is reliable as it is evident from its 'standard error value (0.307).

On comparing the above eqns. (7 and 22), we have found that model derived from partial atomic charges has more reliable predicting power than the model derived from HOMO densities, because the formal model has higher values of r^2, r^2_{CV} and lower value of standard error and used less descriptor than the later model. The current study accounts for the previous findings with advanced approaches (DFT) but in more easier and convenient way. Ivanciuc *et al.* [24] for the first time made QSAR study on these polychlorinated biphenyls aggregated from various literature reports. Predictive ability of their models was 'r' between 0.903 and 0.935 for splinoid QSSAR and 'r' between 0.745 and 0.887 for cluster-expansion [24]. In continuation to this Katritzky *et al.* [20], reported QSAR results of the same data set based on 486 constitutional, topological, geometrical, electrostatic, quantum chemical and thermodynamic descriptors derived solely from molecular structure and calculated using CODESSA Pro software and proposed that two-parameter model satisfactorily describes the relationship between observed and calculated values in terms of statistical parameters. Borges de Melo [46] reported QSAR results based on E-state and topological descriptors using SMILE software and the best model presented five descriptors (one E-state index and four topological descriptors). It has been proven that local atomic charges are important in many chemical reactions and physico-chemical properties of compounds, thus it may also helpful in determining the new methodology of the degradation of polychlorinated biphenyls, which is also a great challenge because these compounds are strongly resistant to destruction due to their high chemical stability [5].

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