Table 1: Biological activity values (pCC_{50}) and structural features of the diarylpyridazine derivatives

No.	R1	R2	pCc_{50}(exp)[5]	pCc_{50}(cal)
1	2,4,6-TriMe	p-Cl	-2.3222	-1.7252
2	2,4,6-TriMe	p-Me	-2.3874	-1.8522
3	2,4,6-TriMe	p-NO2	0.0268	0.7125
4	2,4,6-TriMe	p-CN	-1.5599	-1.0773
5	2,4,6-TriCl	p-CN	-1.2695	-0.6928
6	2,4,6-TriBr	p-CN	-1.3483	-0.6298
7	2,6-DiBr-4-Me	p-CN	-1.2833	-0.7785
8	2,6-DiMe-4-Br	p-CN	-1.9248	-1.1659
9	2,6-DiMeO	p-CN	-0.4624	0.0981
10	2,6-DiCl	p-CN	-1.9689	-1.2998
11	4-CN-2,6-DiMe	p-CN	-1.7259	-0.8598
12	2,6-DiMe	p-CN	-0.4624	-0.1449
A	2,4,6-TriMe	p- Br	---	-0.9335

R1	R2	R3	R4		pCc_{50}(exp)	pCc_{50}(cal)
13	2,4,6-TriMe	p-Cl	H	H	-0.7767	-0.3896
14	2,4,6-TriMe	p-Me	H	H	-2.2672	-1.54959
15	2,4,6-TriMe	p-NO2	H	H	-1.5694	-1.09256
16	2,4,6-TriMe	p-Ome	H	H	0.7694	-0.20987
17	2,4,6-TriMe	p-CN	H	H	-1.6721	-1.01122
18	2,4,6-TriCl	p-CN	H	H	-1.5441	-0.92496
19	2,4,6-TriBr	p-CN	H	H	-2.1431	-1.38065
20	2,6-DiBr-4-Me	p-CN	H	H	-2.1875	-1.57607
21	2,6-DiMe-4-Br	p-CN	H	H	-1.2901	-0.59329
22	2,4,6-TriMe	m-Cl	H	H	-2.0755	-1.34914
23	2,6-DiMe	p-CN	H	H	-2.3117	-1.55314
24	4-CN-2,6-DiMe	p-CN	H	H	-2.4346	-2.06937
25	2,4,6-TriMe	p-CN	Me	H	-2.1554	-1.4929
26	2,4,6-TriMe	p-CN	Me	Me	2.3909	-1.70819
B	2,4,6-TriMe	p- Br	H	H	---	-0.9854

Table2: The calculated quantum chemical descriptors used in this study

Brief Description	*Descriptor*	*Brief Description*	*Descriptor*
Highest Occupied Molecular Orbital	HOMO	Molecular Volume	Vol
Lowest Occupied Molecular Orbital	LUMO	Ionization Potential	IP
Dipole Moment	DP	Electron affinity	EA
Frequency	Freq	Gap energy	Gap
Electronegativity	χ	Surface Area (Approximation)	Sur_{Approx}
Stabilization energy	Hf	Surface Area (Grid)	Sur_{Grid}
Entropy	ΔS	Hydration energy	HE
Gibbs free energy	ΔG	Log p(Solubility)	Log p
Molar heat capacity in constant volume	C_V	Refractivity	Ref
Thermal Free energy	E_T	Hardness	H
Molecular Mass	Mass	Softness	S
Polarizibility	Polar	$-Log(CC_{50})$	pCC_{50}

3. Results and Discussion

In the present study, we tried to develop the best QSAR model to explain the correlation between the quantum chemistry parameters and anti-HIV activity of DAPD compounds. Quantum descriptors of new DAPD derivatives with anti-HIV activity were used for the present QSAR study. After regression analysis by the software SPSS with multilinear regression (MLR), the best equation obtained. The QSAR studies of the DAPD compounds resulted in several QSAR equations. The best equations are:

No	*Formula*
1	pCC_{50}= 4.682+0.002* DP +(-0.182)* $Freq_L$ +0.147*Freq + 0.028* ΔS +4.679* C_V +(-4.094)* Hf +0.002*Mass +0.013* Sur_{Approx} +(-0.020)* Sur_{Grid} +-(0.001)* Vol+ (-0.011)* η + 0.042* HE +(-0.228)*Log p+0.011* Ref +(-0.014)*polar+ 0. 724*s +10.399* IP+(-22.490)* EA R=0.983 R^2=0.966 F= 8.954 S.E=0.258
2	pCC_{50}= 5.316+-0.22* DP +(-0.004)* Freq + 0.020* ΔS +2.69* C_V -4.175* ΔG +-14..848* EA +5.101* Gap +0.001* Mass +0.014* Sur_{Approx} +-0.022* Sur_{Grid} +0.015* Hf +-0.164* Log p +-0.084* Polar +0.001*Pol+0.831*S+-0.011* η R=0.982 R^2=0.964 F= 15.160 S.E=0.216
3	pCC_{50}= 5.670 +(-0.011)* Freq + 0.023* ΔS +5.159* C_V -2.968* ΔG +-13.753* EA +7.741* Gap +0.002* Mass +0.013* Sur_{Approx} +-0.022* Sur_{Grid} +0.029* Hf +-0.212* Log p +-0.101* Polar +0.001*Pol+0.800*S+-0.011* η R=0.981 R^2=0.963 F= 17.306 S.E=0.209
4	pCC_{50}= 5.526 + 0.018* ΔS +3.952* C_V +5.127* Gap +0.001* Mass +0.012* Sur_{Approx} +-0.020* Sur_{Grid} +0.017* Hf +-0.183* Log p +- 0.077* Polar +0.815*S+-0.011* η R=0.981 R^2=0.962 F= 20.048 S.E=0.202
5	pCC_{50}=5.898+0.036* DP +0.026* ΔS +1.55* C_V + +0.013* Sur_{Approx} + (-0.011)* η+(-0.018)* Sur_{Grid} +0.643*homo +(-0.169)* Ref+0.769*S+15.221*Lumo+-0.180* Polar +0.001*Pol+-4.067* ΔH R=0.979 R^2=0.958 F= 21.317 S.E=0.202
6	pCC_{50}=2.440+0.016* DP +0.053* ΔS +1.34* C_V +0.006*Mass + (-0.011)* η+(-0.005)* Sur_{Grid} +-3.697*homo +(-0.089)* Ref+0.701*S+16.788*Lumo+-0.067* Polar +0.001*Pol+-3.051* ΔH R=0.972 R^2=0.945 F= 15.737 S.E=0.234

The best QSAR model has good predictive power in the value of the regression coefficient (R^2), is greater than 0.5. As the value of regression coefficient increases, the predictive power of QSAR model increases. Maximum of predictive power is achieved when the regression coefficient becomes unity. As can be seen, the equation has acceptable quality and the variables used in model 1 can explain 98.3% of the variance in the activity of DAAN derivatives. Values of predicted pCC_{50} of derivatives of diarylpyrimidine have been calculated by substituting the values of descriptors in MLR equations with model 3 and the plot of predicted activity versus observed activity (Figure 2) provides an idea about how well the model predicts the activity of the compounds.

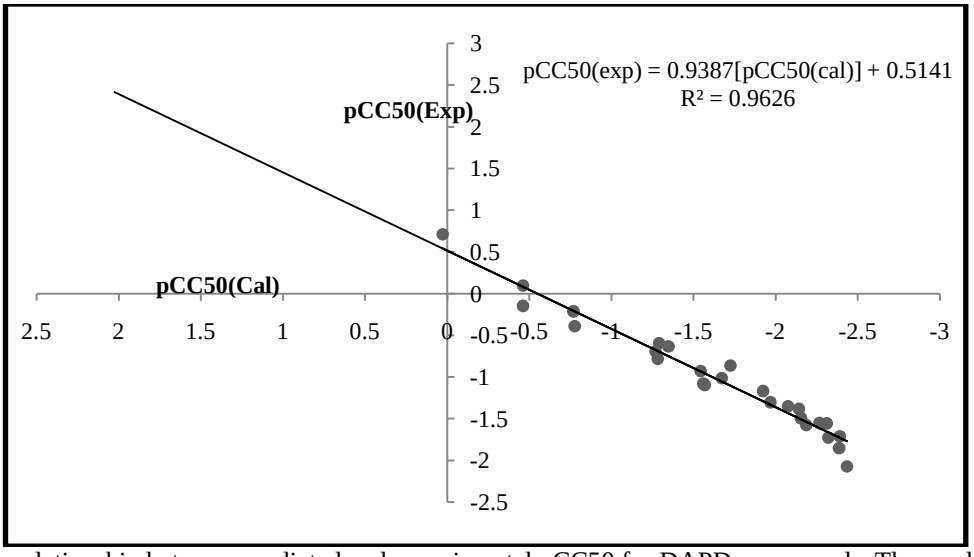

Figure 2: The relationship between predicted and experimental pCC50 for DAPD compounds. The symbols represent experimental pCC50 values.

Values of predicted pCC50 of derivatives of DAPD have been calculated by substituting the values of the described in MLR equations with model 1 and the plot of predicted activity versus observed activity (Figure 2) provides an idea about how well the model was trained and how well it predicts the activity of the compounds. The Compound A of DAPD derivatives (Figure 1, a) with R1=2, 4, 6-TriMe and R2= p- Br and compound B of DAPD derivatives (Figure 1, b) with R1=2, 4, 6-TriMe, R2= p- Br, R3=R4=H were investigated and their quantum mechanics descriptors were extracted. With using of model 1, pCC50 (anti-HIV-1 activity) of these compounds were predicted -0.9335 and -0.9854 respectively in comparison to table 1, is suitable and has anti-HIV activity appropriate.

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