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Lipophilicity Determination for Amino-Drugs Compounds Using Theoretical Calculations

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Abstract

Two set of drugs compounds containing amino group have been determined using (AM1), (PM3) and HartreeFock in basis set (HF/STO-3G). The practical values (Log P) were predicted depending on the physical properties of the drugs compounds. The physico-chemical data were evaluated theoretically (i.e. LUMO, HOMO, entropy, Gibbs free energy, …etc) and used to find the lipophilicity. An excellent correlation was obtained between the theoretical and the experimental values.

Keywords:*LogP, HOMO, LUMO, Amino-Drug, Theoretical Calculations*

1. Introduction:

Lipophilicity is a physic-chemical property in medicinal chemistry. It is an important factor to define pharmaco-kinetics and pharmaco-dynamics of a drug substance[1,2]. The theoretical calculations are used to description for the ionization potential[3], drug design[4,5] metabolite of antipyrine[6] and lipophilicity[7-9] or by experimental methods like UV-VIS and HPLC[10].Lipophilicity with low molecular weight and low polar surface area is the major driving force that leads to good absorption of chemicals in the intestine by passive diffusion. Lipophilicity plays a main role in governing kinetic and dynamic aspects of drug action[11-13].

Lipophilic molecules have higher absorption, penetration into tissues and a wider distribution. The molecules with higher value of lipophilicity is show higher values of plasma protein binding with comparison to the less value of lipophilic compounds at similar properties. Lipophilicity can be characterized by the partition coefficient (logPO/W) in n-octanol/water[14,15].Lipophilicity is a molecular property of immense importance in pharmacy, bio- and medicinal chemistry. Ability of drugs to diffuse passively through biological membranes is influenced to a large extent by their lipophilicity[16].

2. Experimental

ChemBio Office (version 11.0.1) program was used in calculations. The (GAUSSIAN 03W) program was employed for the determinations. The correlation coefficient (R), standard error (SE) and Fisher constant (F) were employed to judge the validity of regression equation. Many sets of drugs were taken which containing amino group on the aliphatic and aromatic compounds.

The physic-chemical properties were calculated include thermodynamic parameters like Free energy (ΔG) , Thermal (ΔH), Entropy (S), steric energy (S.E), mol refractivity (M.R), the highest occupied molecular orbital energy (HOMO), the lowest unoccupied molecular orbital energy (LUMO), Zero-point Energies (Z.P.E), heat of

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formation (H.F), . MM2 method was used to find the best configuration stable form. The minimization is continued until the root mean square (RMS) gradient value reaches a value smaller than0.001 kcal/mol Angstrom. Later, (AM1, PM3 and HF/STO-3G) methods were used to calculate the physical properties of the drugs compounds.

3. Results and Discussion

The two sets of the drugs were shown in the tables (1) and (2) which showed their names, beside the physical parameters which were calculated theoretically using AM1, (PM3) and [HF/STO-3G] methods.

3.1 Set One :

At using the enter method in (SPSS) for all used methods AM1, PM3 and HF/STO-3G, the equations were:

logP = -1.756+ 0.001 (S.E) + 1.746(HOMO) – 4.751(LUMO) + 9.055(F.E) – 0.104(C.V) + 0.037(S) – 0.861(H.F) + 0.306(M.R.) + 0.178(P.C) ------ (AM1)

(No. 15 , R= 0.987 , St. Error = 0.135 , F= 21.60)

logP = -4.189+ 0.002(S.E) – 2.002(HOMO) – 3.549(LUMO) + 13.404(F.E) – 0.182(C.V) + 0.058(S) – 1.746(H.F) + 0.677(M.R.) + 0.125(P.C) ------ (PM3)

(No. 15 , R= 0.997 , St. Error = 0.068 , F= 86.87)

logP = -0.945+ 0.001 (S.E) – 0.287(HOMO) – 2.464(LUMO) + 9.213(F.E) – 0.040(C.V) + 0.022(S) – 0.001(H.F) – 0.254(M.R.) + 0.174(P.C) ------ (HF/STO-3G)

(No. 15 , R= 0.995 , St. Error = 0.087 , F= 51.98)

While at using (stepwise) method, the equations were shown at the following:

logP = -0.857 + 6.382 (F.E) ------ (AM1)

(No. 15 , R= 0.964 , St. Error = 0.140 , F= 170.94)

logP = -0.817 + 6.513 (F.E) ------ (PM3)

(No. 15 , R= 0.966 , St. Error = 0.137 , F= 181.196)

logP = -0.804 + 5.273 (F.E) ------ (HF/STO-3G)

(No. 15 , R= 0.968 , St. Error = 0.132 , F= 194.93)

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Table 1. Set One, The experimental* and the theoretical physical parameters for the Set One using AM1, (PM3) and [HF/STO-3G]

SET ONE	Steric Energy	Log P*	HOMO Hartree	LUMO Hartree	Zero-point Energies Hartree	Thermal Energies Hartree	Enthalpies Hartree	Free Energies Hartree	E Thermal KCal/Mol	CV Cal/Mol-K	S Cal/Mol-K	HF Hartree	Mol Ref#	Partition Coeff#
			-0.30382	0.00319	0.32838	0.34716	0.34810	0.27737	217.84	70.56	148.87	0.15097		0.8057
Abacavir	40.67	0.72	(-0.30658)	(-0.00659)	(0.31583)	(0.33527)	(0.33621)	(0.26497)	(210.38)	(73.91)	(149.95)	(0.06968)	7.8973	
			[-0.22696]	[0.23407]	[0.37352]	[0.39093]	[0.39187]	[0.32474]	[245.31]	[64.58]	[141.28]	[-930.42]		
			-0.36241	-0.0501	0.12651	0.13973	0.14067	0.08464	87.68	46.24	117.93	-0.08220		-0.9808
Acetazolamide	190.82	-0.26	(-0.36456)	(-0.06369)	(0.11920)	(0.13362)	(0.13456)	(0.07435)	(83.848)	(49.82)	(126.72)	(-0.06278)	4.6487	
			[-0.28624]	[0.20365]	[0.13638]	[0.15112]	[0.15207]	[0.09107]	[94.83]	[48.42]	[128.37]	[-1375.63]		
			-0.31470	-0.00177	0.19498	0.20839	0.20934	0.15283	130.77	49.84	118.93	0.08776		0.6136
Apraclonidine	13.58	0.3	(-0.31498)	(-0.00488)	(0.18727)	(0.20139)	(0.20233)	(0.14403)	(126.37)	(52.18)	(122.70)	(0.04757)	6.1828	
			[-0.25218]	[0.22421]	[0.21942]	[0.23228]	[0.23323]	[0.17821]	[145.76]	[46.98]	[115.79]	[-1466.58]		
			-0.37654	-0.06222	0.14807	0.16310	0.16404	0.10426	102.34	56.42	125.83	-0.12886		-0.2940
Chlorothiazide	368.8	-0.18	(-0.36331)	(-0.05799)	(0.13836)	(0.15500)	(0.15594)	(0.09256)	(97.26)	(61.22)	(133.40)	(-0.13882)	6.1401	
			[-0.28858]	[0.14741]	[0.15302]	[0.17038]	[0.17132]	[0.10671]	[106.91]	[60.89]	[136.00]	[-1962.22]		
			-0.32435	0.0089	0.18611	0.19726	0.19821	0.14820	123.78	40.28	105.24	-0.12075		0.1690
Dopamine	-6.82	0.12	(-0.32594)	(0.00731)	(0.18188)	(0.19341)	(0.19436)	(0.14335)	(121.36)	(41.84)	(107.36)	(-0.11477)	4.2911	
			[-0.23195]	[0.26718]	[0.21300]	[0.22313]	[0.22408]	[0.17647]	[140.01]	[37.07]	[100.21]	[-507.05]		
			-0.35899	-0.03833	0.17088	0.18673	0.18767	0.12692	117.17	59.37	127.87	-0.16265		-0.3647
Hydrochloro-thiazide	369.73	-0.07	(-0.35901)	(-0.04526)	(0.16033)	(0.17745)	(0.17840)	(0.11421)	(111.35)	(63.75)	(135.10)	(-0.16161)	6.31750	
			[-0.28741]	[0.18512]	[0.18195]	[0.19964]	[0.20058]	[0.13543]	[125.27]	[62.33]	[137.11]	[-1963.42]		
			-0.33885	0.00545	0.21522	0.22724	0.22818	0.17679	142.59	44.83	108.16	-0.12635		-0.0832
Metaraminol	-0.56	0.07	(-0.34110)	(0.00187)	(0.20976)	(0.22215)	(0.22310)	(0.17129)	(139.40)	(46.80)	(109.04)	(-0.11714)	4.7549	
			[-0.25216]	[0.26095]	[0.24643]	[0.25752]	[0.25846]	[0.20913]	[161.59]	[41.37]	[103.84]	[-545.62]		
			-0.33458	0.00574	0.26377	0.28142	0.28237	0.21308	176.59	62.21	145.82	-0.29670		0.1462
Methocarbamol	4.8	0.55	(-0.35357)	(-0.00304)	(0.25347)	(0.27132)	(0.27226)	(0.20379)	(170.25)	(64.44)	(144.11)	(-0.28075)	6.0244	
			[-0.25157]	[0.25709]	[0.29981]	[0.31621]	[0.31716]	[0.25204]	[198.42]	[57.57]	[137.06]	[-843.13]		
			-0.34735	0.01082	0.35395	0.37270	0.37364	0.30533	233.87	68.62	143.77	0.01183		1.9060
Milnacipran	8.04	1.23	(-0.34491)	(0.00452)	(0.34339)	(0.36220)	(0.36314)	(0.29540)	(227.28)	(71.10)	(142.58)	(-0.00958)	7.4985	
			[-0.26666]	[0.25963]	[0.40960]	[0.42712]	[0.42806]	[0.36237]	[268.02]	[62.83]	[138.26]	[-755.18]		
			-0.32314	0.00055	0.33627	0.35440	0.35535	0.28673	222.39	66.27	144.41	-0.03271		1.4228
Procainamide	7.07	1.23	(-0.32602)	(-0.00567)	(0.32567)	(0.34389)	(0.34484)	(0.27660)	(215.79)	(68.30)	(143.61)	(-0.05502)	7.0770	
			[-0.24489]	[0.23012]	[0.38847]	[0.40551]	[0.40646]	[0.34059]	[254.46]	[61.08]	[138.63]	[-733.56]		
			-0.38407	-0.03216	0.10617	0.11345	0.11439	0.07293	71.191	26.64	87.24	0.00978		-0.6763
Pyrazinamide	3.53	-0.37	(-0.37362)	(-0.03712)	(0.10155)	(0.10911)	(0.11006)	(0.06860)	(68.47)	(27.86)	(87.26)	(-0.00081)	3.1346	
			[-0.31261]	[0.18101]	[0.11695]	[0.12378]	[0.12472]	[0.08506]	[77.67]	[24.97]	[83.47]	[-424.95]		
			-0.37091	-0.02811	0.18545	0.19952	0.20046	0.14096	125.20	51.72	125.22	-0.01704		0.5143
Rufinamide	6.24	0.05	(-0.36230)	(-0.03554)	(0.17873)	(0.19314)	(0.19408)	(0.13412)	(121.19)	(53.54)	(126.19)	(-0.05238)	5.5701	
			[-0.28804]	[0.22218]	[0.20466]	[0.21805]	[0.21899]	[0.16106]	[136.82]	[48.81]	[121.94]	[-863.54]		
			-0.33777	-0.01885	0.27150	0.29133	0.29227	0.22126	182.81	73.03	149.45	-0.10883		1.2312
Sulfadoxine	192.91	0.34	(-0.34039)	(-0.02779)	(0.25893)	(0.27994)	(0.28089)	(0.20683)	(175.66)	(77.33)	(155.87)	(-0.12803)	7.6213	
			[-0.25789]	[0.20804]	[0.29974]	[0.31987]	[0.32081]	[0.24831]	[200.72]	[71.86]	[152.61]	[-1360.21]		
			-0.32119	-0.0004	0.32358	0.34457	0.34551	0.27100	216.22	76.04	156.82	-0.06492		0.9811
Trimethoprim	27.3	0.79	(-0.32252)	(-0.00496)	(0.31183)	(0.33368)	(0.33463)	(0.25594)	(209.38)	(79.02)	(165.61)	(-0.09409)	7.8295	
			[-0.25610]	[0.23299]	[0.36605]	[0.38583]	[0.38678]	[0.31419]	[242.11]	[71.25]	[152.76]	[-970.63]		
			-0.35894	-0.03177	0.16317	0.17505	0.17599	0.12367	109.84	45.04	110.12	-0.01783		-0.3630
Zonisamide	187.5	-0.1	(-0.36160)	(-0.03512)	(0.15563)	(0.16835)	(0.16930)	(0.11502)	(105.64)	(48.32)	(114.23)	(-0.02902)	5.0844	
			[-0.27600]	[0.19559]	[0.17968]	[0.19210]	[0.19304]	[0.13948]	[120.54]	[44.59]	[112.73]	[-1025.77]		

* = Experimental # = Used for all Compounds

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Table 2. Set Two, The experimental* and the theoretical physical parameters for the Set One using AM1, (PM3) and [HF/STO-3G]

SET TWO	Steric Energy	Log P*	HOMOHartree	LUMOHartree	Zero-point EnergiesHartree	Thermal EnergiesHartree	EnthalpiesHartree	Free EnergiesHartree	E ThermalKCal/Mol	CV Cal/Mol-K	S Cal/Mol-K	HF Hartree	Mol Ref#	Partition Coeff#
Chlorphenesin carbamate	5.79	1.41	-0.34025 (-0.33416) [-0.26400]	-0.00137 (-0.00082) [0.24116]	0.22146 (0.21237) [0.25054]	0.23756 (0.22890) [0.26551]	0.23851 (0.22985) [0.26645]	0.17346 (0.16365) [0.20443]	149.07 (143.64) [166.61]	56.91 (59.09) [52.66]	136.90 (139.33) [130.54]	-0.2467 (-0.22916) [-1184.71]	5.8989	1.2602
Dichlorphenamide	365.39	0.93	-0.38368 (-0.36819) [-0.29844]	-0.05402 (-0.05361) [0.16431]	0.13598 (0.12877) [0.14130]	0.15215 (0.14627) [0.15971]	0.15310 (0.14721) [0.16066]	0.09039 (0.08139) [0.09299]	95.48 (91.78) [100.22]	58.49 (62.22) [62.50]	131.99 (138.53) [142.43]	-0.1962 (-0.18402) [-2325.66]	6.1538	0.2413
Guanfacine	15.46	1.12	-0.34695 (-0.33876) [-0.28276]	0.0026 (-0.00520) [0.22327]	0.18030 (0.17452) [0.20162]	0.19462 (0.18910) [0.21496]	0.19556 (0.19004) [0.21590]	0.13510 (0.12953) [0.15863]	122.13 (118.66) [134.89]	51.87 (53.21) [48.69]	127.24 (127.36) [120.53]	-0.0100 (-0.02594) [-1486.07]	6.1792	1.2540
Indapamide	184.67	2.1	-0.33373 (-0.33192) [-0.24123]	-0.03311 (-0.03459) [0.18343]	0.31251 (0.29967) [0.34789]	0.33384 (0.32223) [0.36943]	0.33479 (0.32317) [0.37038]	0.25940 (0.24504) [0.29448]	209.49 (202.20) [231.82]	81.16 (85.64) [78.76]	158.66 (164.46) [159.75]	-0.0312 (-0.06112) [-1837.99]	9.3833	2.9570
Metoclopramide	23.63	2.35	-0.32176 (-0.32280) [-0.25111]	-0.00419 (-0.00734) [0.21764]	0.36019 (0.34675) [0.41575]	0.38200 (0.36966) [0.43624]	0.38295 (0.37061) [0.43719]	0.30580 (0.28973) [0.36311]	239.71 (231.97) [273.75]	78.60 (82.27) [73.31]	162.38 (170.22) [155.90]	-0.1035 (-0.12084) [-1299.98]	8.1853	2.2293
Niacin	17.04	0.82	-0.38860 (-0.39253) [-0.31166]	-0.03590 (-0.03817) [0.19533]	0.10583 (0.10285) [0.11713]	0.11215 (0.11012) [0.12398]	0.11309 (0.11107) [0.12492]	0.07488 (0.07024) [0.08495]	70.38 (69.10) [77.80]	24.16 (27.06) [24.58]	80.43 (85.94) [84.13]	-0.0819 (-0.09098) [-428.72]	3.1301	0.7990
Phenelzine	-17.06	1.14	-0.35024 (-0.32912) [-0.27488]	0.01274 (0.01092) [0.26442]	0.19550 (0.18833) [0.22375]	0.20522 (0.19831) [0.23267]	0.20616 (0.19925) [0.23362]	0.15858 (0.15201) [0.18795]	128.78 (124.44) [146.01]	34.94 (36.81) [31.62	100.14 (99.43) [96.11]	0.0583 (0.06408) [-	4.3536	1.0330

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										]		413.66]		
Pramipexole	**5.55**	**1.62**	**-0.31898 (-0.32429) [-0.24164]**	**-0.00522 (-0.01621) [0.27138]**	**0.27158 (0.26241) [0.31745]**	**0.28590 (0.27715) [0.33063]**	**0.28685 (0.27810) [0.33157]**	**0.22840 (0.21882) [0.27639]**	**179.41 (173.92) [207.47]**	**52.56 (55.22) [48.05]**	**123.01 (124.77) [116.14]**	**0.0209 (0.0240 1) [- 938.41]**	**6.093 2**	**1.1680**
Primaquine	**15.91**	**2.67**	**-0.29501 (-0.30190) [-0.20922]**	**-0.00968 (-0.01990) [0.20440]**	**0.35094 (0.33962) [0.40330]**	**0.36983 (0.35876) [0.42073]**	**0.37078 (0.35970) [0.42167]**	**0.30089 (0.29015) [0.35554]**	**232.07 (225.13) [264.01]**	**69.35 (71.87) [63.64]**	**147.10 (146.38) [139.18]**	**-0.0054 (- 0.01509) [- 808.39]**	**7.838 8**	**2.5982**
Tranylcypromin e	**6.79**	**1.21**	**-0.33865 (-0.34072) [-0.26164]**	**0.01547 (0.01021) [0.26395]**	**0.18437 (0.17831) [0.21037]**	**0.19307 (0.18730) [0.21827]**	**0.19401 (0.18824) [0.21921]**	**0.15009 (0.14350) [0.17686]**	**121.15 (117.53) [136.97]**	**33.32 (34.61) [29.53]**	**92.45 (94.16) [89.14]**	**0.0716 (0.0717 6) [- 396.73]**	**4.311 3**	**1.4780**
Triamterene	**33.15**	**1.3**	**-0.31304 (-0.31837) [-0.24186]**	**-0.01711 (-0.03192) [0.17106]**	**0.23733 (0.23027) [0.26293]**	**0.25273 (0.24590) [0.27671]**	**0.25367 (0.24684) [0.27766]**	**0.19434 (0.18607) [0.22187]**	**158.59 (154.31) [173.64]**	**60.39 (61.62) [55.26]**	**124.89 (127.92) [117.41]**	**0.1947 (0.1308 3) [- 831.43]**	**7.149 5**	**1.6076**

* = Experimental # = Used for all Compounds

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Table 3. The binary correlations between parameters for set one using (AM1)

SET ONE	S.E	LogP	M.R.	P.C	HOMO	LUMO	Z.P.E	T.E	Enth.	F.E	E	CV	S	HF
S.E	1													
LogP	-0.457	1												
M.R	0.072	0.755	1											
P.C	-0.414	0.899	0.775	1										
HOMO	-0.453	0.657	0.552	0.569	1									
LUMO	-0.786	0.721	0.318	0.652	0.784	1								
Z.P.E	-0.402	0.962	0.829	0.892	0.692	0.718	1							
T.E	-0.384	0.96	0.841	0.891	0.689	0.705	1	1						
Enth.	-0.384	0.959	0.841	0.891	0.689	0.705	1	1	1					
F.E	-0.424	0.964	0.81	0.895	0.696	0.737	0.999	0.998	0.998	1				
E	-0.384	0.959	0.841	0.891	0.689	0.705	1	1	1	0.998	1			
CV	0.087	0.742	0.974	0.726	0.51	0.305	0.831	0.844	0.844	0.809	0.844	1		
S	0.007	0.757	0.94	0.707	0.517	0.327	0.831	0.845	0.845	0.807	0.845	0.984	1	
HF	-0.288	0.198	0.179	0.297	0.235	0.124	0.172	0.163	0.163	0.185	0.163	-0.01	-0.046	1

S.E: Steric Energy , M.R.= Molar Refractivity, P.C.= Partition coefficient, Z.P.E.= Zero Point Energy, T.E.= Thermal Energy
Enth.= Enthalpy, F.E. = Free Energy, E= Energy, S= Entropy, H.F= heat of formation

Table 4. The binary correlations between parameters for set one using (PM3)

SET ONE	S.E	LogP	M.R.	P.C	HOMO	LUMO	Z.P.E	T.E	Enth.	F.E	E	CV	S	HF
S.E	1													
LogP	-0.457	1												
M.R	0.072	0.755	1											
P.C	-0.414	0.899	0.775	1										
HOMO	-0.436	0.633	0.564	0.614	1									
LUMO	-0.76	0.693	0.291	0.641	0.723	1								
Z.P.E	-0.421	0.964	0.817	0.894	0.666	0.696	1							
T.E	-0.398	0.961	0.832	0.893	0.663	0.679	1	1						
Enth.	-0.398	0.961	0.832	0.893	0.663	0.679	1	1	1					
F.E	-0.453	0.966	0.789	0.896	0.67	0.723	0.998	0.996	0.996	1				
E	-0.398	0.961	0.832	0.893	0.663	0.679	1	1	1	0.996	1			
CV	0.151	0.703	0.972	0.691	0.452	0.212	0.783	0.802	0.802	0.75	0.802	1		
S	0.134	0.661	0.933	0.626	0.426	0.159	0.734	0.754	0.754	0.696	0.754	0.981	1	
HF	-0.285	0.121	0.053	0.207	0.338	0.071	0.078	0.067	0.067	0.097	0.067	-0.143	-0.186	1

Table 5. The binary correlations between parameters for set one using (HF/STO-3G)

SET ONE	S.E	LogP	M.R.	P.C	HOMO	LUMO	Z.P.E	T.E	Enth.	F.E	E	CV	S	HF
S.E	1													
LogP	-0.457	1												
M.R	0.072	0.755	1											
P.C	-0.414	0.899	0.775	1										
HOMO	-0.439	0.619	0.468	0.54	1									
LUMO	-0.772	0.58	0.154	0.494	0.722	1								
Z.P.E	-0.439	0.968	0.803	0.891	0.676	0.608	1							
T.E	-0.415	0.966	0.818	0.891	0.67	0.592	1	1						
Enth.	-0.415	0.966	0.818	0.891	0.67	0.592	1	1	1					
F.E	-0.472	0.968	0.777	0.891	0.683	0.629	0.999	0.997	0.997	1				
E	-0.415	0.966	0.818	0.891	0.67	0.592	1	1	1	0.997	1			
CV	0.308	0.595	0.94	0.594	0.319	0.004	0.654	0.677	0.677	0.619	0.677	1		
S	0.305	0.567	0.902	0.538	0.278	-0.009-	0.614	0.638	0.638	0.576	0.638	0.986	1	
HF	-0.869	0.28	-0.294	0.216	0.28	0.659	0.296	0.27	0.27	0.334	0.27	-0.461	-0.467	1

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Table (6) was show the experimental and the predicted values of (logP) for the (15) drugs using the stepwise equation. The correlation shows an excellent predicted for the drugs about (R=0.964) for all methods.

Table 6. Experimental and predicted of logP using all methods

Drugs	Log P (Practical)	AM1		PM3		HF/STO-3G	
SET ONE		Log P (Predicted)	Residuals	Log P (Predicted)	Residuals	Log P (Predicted)	Residuals
Abacavir	0.72	0.91	0.19	0.91	0.19	0.91	0.19
Acetazolamide	-0.26	-0.32	-0.06	-0.33	-0.07	-0.32	-0.06
Apraclonidine	0.3	0.12	-0.18	0.12	-0.18	0.14	-0.16
Chlorothiazide	-0.18	-0.19	-0.01	-0.21	-0.03	-0.24	-0.06
Dopamine	0.12	0.09	-0.03	0.12	0.00	0.13	0.01
Hydrochlorothiazide	-0.07	-0.05	0.02	-0.07	0.00	-0.09	-0.02
Metaraminol	0.07	0.27	0.20	0.30	0.23	0.30	0.23
Methocarbamol	0.55	0.50	-0.05	0.51	-0.04	0.52	-0.03
Milnacipran	1.23	1.09	-0.14	1.11	-0.12	1.11	-0.12
Procainamide	1.23	0.97	-0.26	0.98	-0.25	0.99	-0.24
Pyrazinamide	-0.37	-0.39	-0.02	-0.37	0.00	-0.36	0.01
Rufinamide	0.05	0.04	-0.01	0.06	0.01	0.05	0.00
Sulfadoxine	0.34	0.56	0.22	0.53	0.19	0.51	0.17
Trimethoprim	0.79	0.87	0.08	0.85	0.06	0.85	0.06
Zonisamide	-0.1	-0.07	0.03	-0.07	0.03	-0.07	0.03
R		0.964		0.966		0.968	

3.2 Set two:

At using the enter method in (SPSS) for all used methods AM1, PM3 and HF/STO-3G, the equations were:

logP = 2.873+0.001(S.E)+11.120(HOMO)–9.165(LUMO)+3.627(F.E)–0.031(C.V) + 0.042(S) – 0.452(M.R.) + 0.529(P.C) ------ (AM1)
(No. 11 , R= 1.00 , St. Error = 0.009 , F= 4716.95)

logP = 1.093+0.003(S.E)+13.004(HOMO)–17.231(LUMO)+8.694(F.E)–0.164(C.V)+0.086(S) + 0.036(M.R.) + 0.585(P.C) ------ (PM3)
(No. 11 , R= 1.00 , St. Error = 0.04 , F= 272.57)

logP = 3.262 + 2.94x10-5(S.E) + 7.272(HOMO) – 7.901(LUMO) + 9.091(F.E) – 0.064(C.V) + 0.029(S) – 0.240(M.R.) + 0.278(P.C) – 0.001(HF) ------ (HF/STO-3G)
(No. 11 , R= 1.00 , St. Error = 0.029 , F= 481.39)

While at using (stepwise) method, the equations were shown at the following:

logP = -0.097 + 6.950 (Z.P.E) ------ (AM1)
(No. 11 , R= 0.964 , St. Error = 0.180 , F= 103.88)

logP = -0.129 + 6.867(Thermal .E) ------ (PM3)
(No. 11 , R= 0.963 , St. Error = 0.170 , F= 116.35)

logP = -0.067 + 5.711 (Thermal .E) ------ (HF/STO-3G)
(No. 11 , R= 0.963 , St. Error = 0.171 , F= 115.34)

Table 7. The binary correlations between parameters for set two using (AM1)

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SETTWO	S.E	LogP	M.R.	P.C	HOMO	LUMO	Z.P.E	T.E	Enth.	F.E	E	CV	S	HF
S.E	1													
LogP	-0.128	1												
M.R	0.288	0.776	1											
P.C	-0.187	0.869	0.759	1										
HOMO	-0.431	0.777	0.614	0.723	1									
LUMO	-0.798	0.118	-0.2	0.151	0.46	1								
Z.P.E	-0.186	0.964	0.814	0.853	0.852	0.211	1							
T.E	-0.159	0.963	0.831	0.851	0.844	0.189	0.999	1						
Enth.	-0.167	0.963	0.831	0.852	0.844	0.198	0.999	1	1					
F.E	-0.226	0.961	0.783	0.856	0.864	0.24	0.998	0.996	0.996	1				
E	-0.159	0.963	0.831	0.851	0.844	0.189	0.999	1	1	0.996	1			
CV	0.329	0.768	0.982	0.685	0.559	-0.231	0.8	0.82	0.823	0.765	0.82	1		
S	0.297	0.758	0.944	0.632	0.525	-0.171	0.784	0.805	0.818	0.745	0.805	0.984	1	
HF	-0.401	0.01	-0.011	0.229	0.45	0.37	0.118	0.099	0.096	0.157	0.099	-0.165	-0.284	1

Table 8. The binary correlations between parameters for set two using (PM3)

SET TWO	S.E	LogP	M.R.	P.C	HOMO	LUMO	Z.P.E	T.E	Enth.	F.E	E	CV	S	HF
S.E	1													
LogP	-0.128	1												
M.R	0.288	0.776	1											
P.C	-0.187	0.869	0.759	1										
HOMO	-0.362	0.723	0.617	0.65	1									
LUMO	-0.726	0.069	-0.252	0.101	0.415	1								
Z.P.E	-0.197	0.963	0.809	0.854	0.822	0.148	1							
T.E	-0.165	0.963	0.829	0.852	0.814	0.125	0.999	1						
Enth.	-0.165	0.963	0.829	0.852	0.814	0.125	0.999	1	1					
F.E	-0.246	0.96	0.773	0.856	0.833	0.181	0.998	0.994	0.994	1				
E	-0.165	0.963	0.829	0.852	0.814	0.125	0.999	1	1	0.994	1			
CV	0.354	0.766	0.978	0.679	0.542	-0.284	0.786	0.81	0.81	0.743	0.81	1		
S	0.347	0.732	0.937	0.61	0.494	-0.234	0.749	0.774	0.774	0.701	0.774	0.986	1	
HF	-0.432	-0.03	-0.105	0.16	0.392	0.277	0.083	0.057	0.057	0.134	0.057	-0.281	-0.404	1

Table 9. The binary correlations between parameters for set two using (HF/STO-3G)

SET TWO	S.E	LogP	M.R.	P.C	HOMO	LUMO	Z.P.E	T.E	Enth.	F.E	E	CV	S	HF
S.E	1													
LogP	-0.128	1												
M.R	0.288	0.776	1											
P.C	-0.187	0.869	0.759	1										
HOMO	-0.262	0.843	0.683	0.786	1									
LUMO	-0.645	-0.04	-0.411	-0.112	0.093	1								
Z.P.E	-0.228	0.961	0.783	0.841	0.88	0.079	1							
T.E	-0.195	0.963	0.803	0.841	0.874	0.053	0.999	1						
Enth.	-0.195	0.963	0.803	0.841	0.874	0.053	0.999	1	1					
F.E	-0.275	0.955	0.75	0.839	0.888	0.116	0.998	0.995	0.995	1				
E	-0.195	0.963	0.803	0.841	0.874	0.053	0.999	1	1	0.995	1			
CV	0.466	0.696	0.961	0.606	0.52	-0.499	0.679	0.705	0.705	0.635	0.705	1		
S	0.489	0.672	0.915	0.545	0.442	-0.449	0.641	0.669	0.669	0.594	0.669	0.985	1	
HF	-0.824	-0.097	-0.577	-0.015	0.096	0.541	-0.051	-0.088	-0.088	0.006	-0.088	-0.732	-0.776	1

Table (10) was show the predicted of the (11) drugs. The correlation between the experimental and the predicted values shows an excellent predicted for the drugs about (R=0.963) for all methods.

Table 10. Experimental and predicted of logP using all method

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Drugs	Log P(Practical)	AM1 Log P		PM3Log P		HF/STO-3GLog P	
SET TWO		(Predicted)	Residuals	(Predicted)	Residuals	(Predicted)	Residuals
Chlorphenesincarbamate	1.41	1.44	1.41	1.44	0.03	1.45	0.04
Dichlorphenamide	0.93	0.85	0.93	0.88	-0.05	0.85	-0.08
Guanfacine	1.12	1.16	1.12	1.17	0.05	1.16	0.04
Indapamide	2.1	2.07	2.1	2.08	-0.02	2.04	-0.06
Metoclopramide	2.35	2.41	2.35	2.41	0.06	2.42	0.07
Niacin	0.82	0.64	0.82	0.63	-0.19	0.64	-0.18
Phenelzine	1.14	1.26	1.14	1.23	0.09	1.26	0.12
Pramipexole	1.62	1.79	1.62	1.77	0.15	1.82	0.20
Primaquine	2.67	2.34	2.67	2.33	-0.34	2.34	-0.33
Tranylcypromine	1.21	1.18	1.21	1.16	-0.05	1.18	-0.03
Triamterene	1.3	1.55	1.3	1.56	0.26	1.51	0.21
R		0.964		0.963		0.963	

4. Conclusion

The computational programs have been selected to obtain the theoretical parameters. The computational tools can be performed by comparison of predicted properties of the drugs with the experimental values. These methods of the database will serve as a useful for developing models.

There is no difference in correlation coefficient for set one about (R=0.964) for all methods AM1, PM3 and (HF/STO-3G). But the fisher factor is about (169.82), (179.47) and (194.34) respectively. So, the HF/STO-3G is the best method to predict the logP values for set one.Also, no difference in correlation coefficient for set two about (R=0.963) for all methods AM1, PM3 and (HF/STO-3G). The fisher factor is about (116.92), (116.49) and (118.17) respectively. So, the HF/STO-3G is the best method to predict the logP values for set two.

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