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Research Article

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A QSAR Approach for the Prediction of Anti-Ulcer Activity of *N*-Acyl Amino Acids and Imidazopyrazines/Pyridines Derivatives

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ABSTRACT

Quantitative Structure-Activity Relationship (QSAR) studies were performed on a series of N-acyl amino acids and imidazopyrazines/pyridines derivatives with the help of PM5 calculations and geometry optimizations using Cache software. Multiple Linear Regression (MLR) analysis was performed to derive QSAR models using the descriptors, molecular weight (M_W), conformation minimum energy (ε), HOMO energy (ε_{HOMO}), solvent accessibility surface area (SASA), molar volume (MV), molar refractivity (MR), LogP (LP) and parachor (Pc). The QSAR model equations of anti-ulcer agents have been developed by using maximum of seven descriptors, in which conformation minimum energy, molar volume and parchor were present have an excellent predictive powers of correlation and cross validation coefficients. These models can successfully predict the anti-ulcer activity of any newly discovered N-acyl amino acids and imidazopyrazines/pyridines derivatives which can later be tested in laboratory.

Key Words: Anti-ulcer activity, PM5, MLR, QSAR models.

INTRODUCTION

The peptic ulcer and related diseases encompass a broad spectrum of clinical disorders ranging from intense burning pain to severe complications such as deep ulcers, strictures etc. The mammalian stomach is a specialized organ of the digestive tract that serves to store and process the food for absorption by intestine. The physiological studies [1] regarding acid secretory pathway have proved that proton pump being the ultimate mediator of acid secretion, is localized in specialized acid secreting tubulovesicular system of the parietal cells in the gastric mucosa. Upon stimulation, however, this system undergoes various morphological changes accompanying oxygen consumption, which elicit acid secretory response. The first medicinal target to be identified was the histamine-2 receptor, the major activating parietal cell receptor. The second medicinal target was the stomach acid pump, the gastric (H^+/K^+)-ATPase. Since proton transport by the gastric (H^+/K^+)-ATPase is the final step in acid secretion, it was anticipated that drugs inhibiting this step could be more effective inhibitors of acid secretion [2]. Such drugs are called proton pump inhibitors (PPI) and they suppress the enzymatic reaction with irreversible formation of covalent bond between enzyme and cysteine disulphide (-S-S-) bond of H^+/K^+-ATPase (proton pump) at secretary surface of the gastric parietal cell. The formation of disulphide bonds is irreversible so new enzyme must be synthesized to resume gastric acid secretion resulting in its suppression. Omeprazole was the first clinically useful compound of this class and was introduced in 1989 [3], has a benzimidazole core. The other commonly used PPIs are lansoprazole, pantoprazole, timoprazole and rabeprazole, all have a benzimidazole nucleus. A newer PPI, tenatoprazole has an imidazopyridine ring instead of a benzimidazole ring. The available anti-ulcer drugs have shortcomings regarding tolerability and efficacy and therefore, the need for new derivatives with similar therapeutic activity but lower toxicity to human beings prevails with the help of computational chemistry techniques.

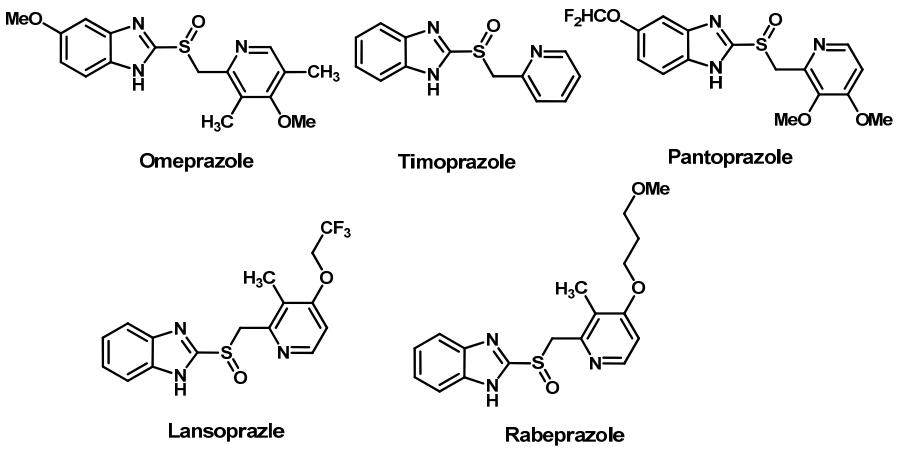


Figure 1: Structures of some widely used proton pump inhibitors having benzimidazole nucleus

In recent time "QSAR Study (Quantum Structural-Activity Relationship)" has found a lot of applications in evaluating relationship between biological activity and molecular structure [4]. This method can afford the luxury of hoping that the properties and interactions of medicinal agents and biological systems can be described by theoretical calculations and a new field has been developed which is progressing with quick speed and is termed as "Quantum Biology," including the areas of mathematics, physics, chemistry, molecular biology and computer technology [5-10].

QSAR analysis in computational research is responsible for the generation of models to correlate biological activity and physiochemical properties of a series of compounds. Latest advances in quantum chemistry using *abinito* and semi-empirical method have made it possible to calculate various physicochemical, quantum mechanical and topological parameters such as molecular weight, polarizability, dielectric constant, molecular refractivity, molar volume, dipole moment, density, surface tension, parachor, HOMO (Highest Occupied Molecular Orbital), LUMO (Lowest Unoccupied Molecular orbital), chemical potential, total energy, core-core repulsion, electron density, shape Index, solvent accessibility surface area (SASA), electronegativity, electrophilicity index, conformation minimum energy, etc. almost to the perfection [11-22].

In current study, a correlation of activity of anti-ulcer derivatives with selected descriptors will be examined and discuss with the help of QSAR techniques using Multiple Linear Regression (MLR) analysis [23,24]. MLR attempts to model the relationship between two or more explanatory variables by fitting a linear equation in observed data. The values of the descriptors will be used to prepare the regression equation and the predicted activity will be obtained from corresponding regression model, and compare with the observed activity. The correlation coefficient and cross validation coefficient will be evaluated so that the quality of relationship may be worked out.

In an effort to find potent drug for anti-ulcer series, we found that *N*-acylderivatives of amino acid [25] and imidazopyrazine/pyridine [26,27] derivatives have shown an excellent activity. The compounds of this series are a class of compounds with reversible and selective inhibitory action of the enzyme (H^+/K^+)-ATPase. The recently published results opened the possibilities of advances for the attainment of the QSAR models.

EXPERIMENT SECTION

The experimental -logIC_{50}(μM) of anti-ulcer activities of *N*-acyl amino acids and imidazopyrazines/pyridines derivatives are collected from literatures [25-27] and are placed in Tables 1-7. The –logIC_{50} can be defined as, "*It is* n*egative* of *logIC_{50} value and because of negative sign, its magnitude has an inverse relationship with the biological activity or drug potency of the selected molecules".* Consequently a low magnitude of -logIC_{50} predicts a higher biological value and a high magnitude of -logIC_{50} indicates lower potency.

QSAR studies of the compounds listed in Tables 1-7 have been made with the help of following descriptors [28-32] using PM5 based calculations.

1. Molecular weight	M_W
2. Conformation minimum energy	ε
3. HOMO energy	ε_{HOMO}
4. Molar volume	MV
5. Molar refractivity	MR
6. LogP	LP
7. Parachor	Pc
8. Solvent accessibility surface area	SASA

The values of the descriptors have been used to prepare Multiple Linear Regression (MLR) equations for predicted activities and compared with the known activity. The correlation coefficient and cross-validation coefficient have been evaluated to adjudge the quality of QSAR model and its predictive power.

RESULT AND DISCUSSION

In this paper, 51 derivatives of *N*-acyl amino acids and imidazopyrazines/pyridines derivatives have been subjected to QSAR analysis in order to find regression equations correlating the biological activity and structure by using selected descriptors. The structures of *N*-acyl amino acids and imidazopyrazines/pyridines derivatives are placed in Tables 1-7, which are presented below.

Table 1: Amino acid derivatives and their observed anti-ulcer activities -logIC_{50} (obs)

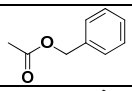
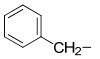
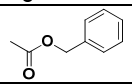
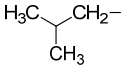
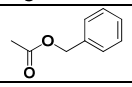
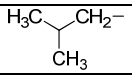
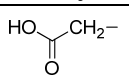
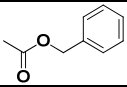
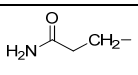
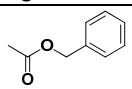
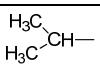
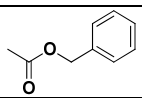
Comp	Parent Structure 		
	R	**R^1**	**H^+/K^+-ATPase (-logIC_{50}) obs**
1	CH_3		-0.37
2			-0.07
3			0.10
4			0.16
5			-0.18
6			-0.75
7			0.12

Table 2: Amino acid derivatives and their observed anti-ulcer activities -logIC_{50}(obs)

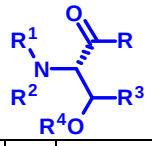
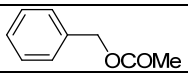
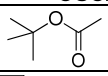
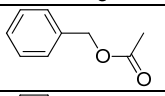
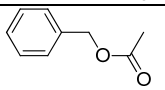
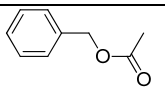
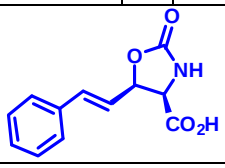
Comp	Parent Structure 					
	R	**R^1**	**R^2**	**R^3**	**R^4**	**H^+/K^+-ATPase (-logIC_{50}) obs**
8	H		H	H	H	-0.95
9	H		H	H	H	0.16
10	H		H	H	Bn	-0.31
11	Et		H	PhCH=CH-	H	0.27
12	Et		H	$Me_3SiC\equiv C-$	H	-0.95
13						0.16

Table 3: Amino acid derivatives and their observed anti-ulcer activities -logIC_{50} (obs)

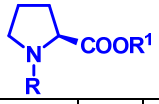
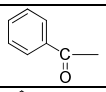
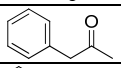
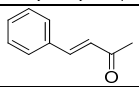
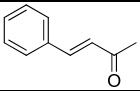
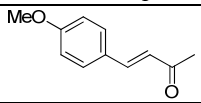
Comp	Parent Structure 		
	R	**R^1**	**H^+/K^+-ATPase (-logIC_{50}) obs**
14	CO_2Et	CH_3	0.21
15		CH_3	1.00
16		H	1.06
17		H	0.14
18		CH_3	0.21
19		CH_3	0.03

Table 4: Amino acid derivatives and their observed anti-ulcer activities -logIC_{50}(obs)

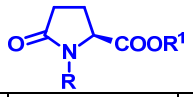
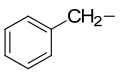
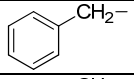
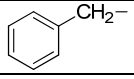
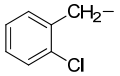
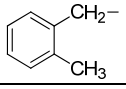
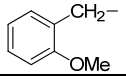
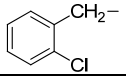
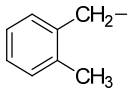
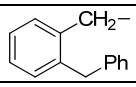
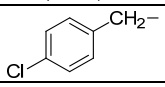
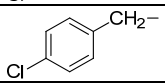
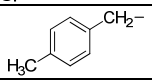
Comp	Parent Structure 		
	R	**R^1**	**H^+/K^+-ATPase (-logIC_{50}) obs**
20	H	H	0.31
21			0.87
22		H (*S-isomer*)	0.33
23		H (*R-isomer*)	0.03
24			0.33
25			1.06
26			-0.12
27		H	0.00
28		H	-0.33
29		H	-0.07
30		H	0.39
31		H	0.03
32		CH_3	-0.07
33			0.58

Table 5: Amino acid derivatives and their observed anti-ulcer activities -logIC_{50}(obs)

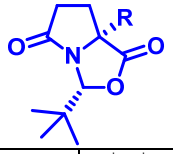
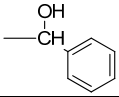
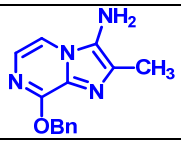
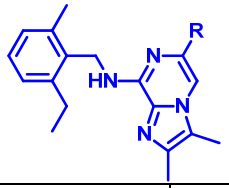
Comp	Parent Structure 	
	R	**H^+/K^+-ATPase (-logIC_{50}) obs**
34	H	0.81
35		-0.10
36		0.09

Table 6: Imidazopyrazine derivatives and their observed anti-ulcer activities -logIC_{50}(obs)

Comp	Chemical Structure	H^+/K^+-ATPase (-logIC_{50}) obs
37		5.9
	Parent Structure 	
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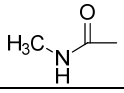
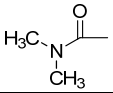
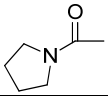
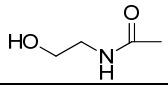
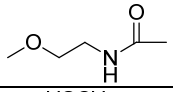
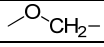
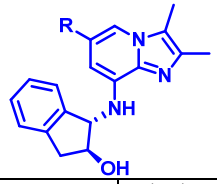
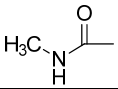
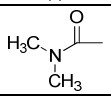
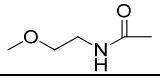
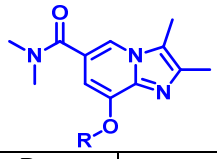
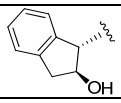
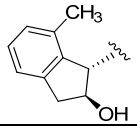
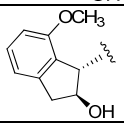
38		5.5
39		6.4
40		6.9
41		5.0
42		6.0
43	$HOCH_2-$	5.9
44		5.5

Table 7: Imidazopyridine derivatives and their observed anti-ulcer activities -logIC_{50}(obs)

Comp	Parent Structure 	
	R	**H^+/K^+-ATPase (-logIC_{50}) obs**
45		4.8
46		5.4
47		6.3
48		4.7
	Parent Structure 	
	R	
49		5.7
50		6.9
51		5.7

MOPAC 2000 engine was used for calculating the value of descriptors of *N*-acyl aminoacid and imidazopyrazine/pyridine derivatives after optimizing the geometry by using PM5 Hamiltonian. These values are presented in table-5.

Descriptors in different combinations have been used for Multiple Linear Regression (MLR) analysis. The predicted activity obtained by regression equation has been examined for selected QSAR models, which have high degree of predictive power; the correlation coefficient and cross validation coefficient of all the regression equations have been evaluated. The best QSAR model and the combination of descriptors providing that model have been identified. Values of quantum chemical and topological descriptors of anti-ulcer agents are included in Table 8.

Table 8: The values of quantum chemical and topological descriptors for anti-ulcer agents

Comp	ε	ε_{HOMO}	Mw	SASA	MV	Pc	MR	LogP
1	-162.205	-9.712	223.228	113.329	179.0	179.0	56.42	1.36
2	-137.191	-9.570	299.326	144.012	239.7	239.7	80.72	3.03
3	-177.261	-9.703	265.308	132.027	228.9	228.9	70.4	2.59
4	-226.470	-10.244	231.291	117.474	217.8	217.8	59.93	1.73
5	-251.372	-9.725	267.238	125.027	190.2	190.2	61.65	0.58
6	-213.191	-9.797	280.280	136.451	212.8	212.8	68.65	0.2
7	-174.062	-9.672	251.282	123.983	212.4	212.4	65.8	2.24
8	-202.571	-9.695	239.227	117.141	176.5	176.5	57.79	0.5
9	-248.929	-10.281	205.210	100.951	165.4	165.4	47.32	-0.36
10	-171.265	-9.535	329.352	142.882	262.6	262.6	87.05	2.59
11	-166.630	-9.134	369.416	174.721	304.1	304.1	102.98	3.33
12	-211.349	-9.712	363.485	176.284	320.3	320.3	91.251	1.078
13	-136.159	-9.407	233.223	109.737	162.6	162.6	60.2	1.27
14	-186.695	-9.813	201.222	103.147	171.5	171.5	49.68	0.44
15	-110.367	-9.623	233.266	113.460	194.4	194.4	63.05	1.41
16	-122.067	-9.245	233.266	113.127	183.9	183.9	61.93	1.09
17	-103.677	-9.324	245.277	120.960	192.1	192.1	68.38	1.49
18	-96.486	-9.313	259.304	128.906	217.5	217.5	73.82	1.75
19	-152.550	-8.672	277.319	133.478	233.3	233.3	74.61	1.23
20	-143.523	-10.296	129.115	70.692	93.4	93.4	27.83	-1.16
21	-132.150	-9.494	275.347	123.954	241.7	241.7	76.79	1.95
22	-116.500	-9.624	219.240	102.506	166.8	166.8	57.33	0.81
23	-116.500	-9.624	219.240	102.067	166.8	166.8	57.33	0.81
24	-139.503	-9.494	309.792	136.242	253.7	253.7	81.4	2.51
25	-138.673	-9.271	289.374	131.637	258.0	258.0	82.69	2.44
26	-167.421	-9.581	227.303	109.803	215.5	215.5	61.79	0.87
27	-153.876	-9.625	249.266	111.007	190.8	190.8	64.58	0.69
28	-123.810	-9.605	253.685	113.229	178.7	178.7	61.94	1.37
29	-122.967	-9.361	233.266	108.999	183.1	183.1	63.23	1.3
30	-97.641	-9.046	309.364	132.533	246.2	246.2	87.53	2.9
31	-124.352	-9.553	253.685	113.718	178.7	178.7	61.94	1.37
32	-118.212	-9.515	267.712	122.070	204.1	204.1	52.47	0.02
33	-140.395	-9.248	289.374	131.694	258.0	258.0	82.69	2.44
34	-146.052	-10.372	197.233	93.438	165.1	165.1	50.21	1.3
35	-165.894	-9.784	303.357	122.909	238.9	238.9	80.3	2.55
36	-137.627	-7.943	295.378	129.938	241.8	241.8	76.66	2.27
37	49.069	-8.720	254.291	125.580	195.0	195.0	73.19	1.97
38	12.870	-8.494	351.450	167.373	291.4	291.4	105.64	3.5
39	20.079	-8.457	365.477	173.228	312.7	312.7	110.64	3.74
40	10.766	-8.421	391.515	181.400	318.1	318.1	117.97	4.05
41	5.530	-8.478	365.477	176.826	305.6	305.6	111.81	2.98
42	-28.787	-8.554	395.503	187.322	330.0	330.0	116.57	3.34
43	8.867	-8.301	324.425	155.071	271.6	271.6	98.7	3.78
44	13.948	-8.268	338.452	163.141	296.0	296.0	103.45	4.15
45	-25.093	-8.323	336.393	150.096	234.1	234.1	96.61	1.49
46	-17.540	-8.474	350.419	158.747	257.2	257.2	101.61	1.73
47	0.746	-8.020	364.446	155.939	278.5	278.5	106.61	1.96
48	-61.925	-8.482	394.472	176.308	295.8	295.8	112.53	1.57
49	78.290	-8.586	365.431	159.281	280.3	280.3	104.67	2.34
50	37.030	-8.569	379.458	168.154	295.5	295.5	110.57	2.83
51	-6.078	-8.429	395.457	181.892	301.9	301.9	111.92	2.21

Comp = Compound, ε = Conformation minimum energy (kcal/mole), Mw = Molecular weight, ε_{HOMO} = HOMO energy, MR = Molar refractivity, SASA = Solvent accessibility surface area, MV = Molar volume, Pc = Parachor

We have also calculated the predicted activity of anti-ulcer agents PA1-PA5 by substituting the values of descriptors in MLR equations. These values are listed in Table-9.

Table 9: Calculated predicted activities from regression equations PA1 to PA5

Comp	PA1	PA2	PA3	PA4	PA5	Obs. Activity -logIC_{50}
1	0.413	0.408	0.329	0.334	0.331	-0.37
2	0.536	0.575	0.484	0.597	0.609	-0.07
3	0.072	0.082	0.021	0.053	0.055	0.10
4	-0.483	-0.457	-0.446	-0.571	-0.562	0.16
5	-1.374	-1.396	-1.447	-1.731	-1.739	-0.18
6	-1.037	-1.023	-1.203	-0.765	-0.759	-0.75
7	0.214	0.214	0.186	0.097	0.095	0.12
8	-0.561	-0.576	-0.676	-0.599	-0.604	-0.29
9	-1.117	-1.109	-1.109	-1.250	-1.246	-0.16
10	-0.107	-0.077	0.063	-0.349	-0.338	-0.31
11	0.490	0.503	0.377	0.770	0.773	0.27
12	-0.377	-0.350	-0.520	-0.163	-0.151	-0.95
13	0.308	0.298	0.260	0.315	0.310	0.16
14	0.240	0.218	0.189	0.154	0.146	0.21
15	1.192	1.209	1.199	1.328	1.334	1.00
16	0.304	0.278	0.209	0.629	0.619	1.06
17	0.732	0.737	0.607	1.269	1.269	0.14
18	1.314	1.324	1.204	1.852	1.854	0.21
19	0.774	0.680	0.627	0.947	0.913	0.03
20	0.601	0.621	0.574	0.613	0.623	0.31
21	0.409	0.425	0.549	0.623	0.629	0.87
22	0.350	0.364	0.373	0.550	0.555	0.33
23	0.342	0.356	0.373	0.532	0.538	0.03
24	0.935	0.957	1.116	0.519	0.527	0.33
25	0.508	0.505	0.614	0.768	0.766	1.06
26	0.330	0.305	0.384	0.517	0.509	-0.12
27	0.105	0.113	0.199	0.112	0.116	0.00
28	-1.048	-1.020	-1.029	-0.918	-0.908	-0.33
29	0.434	0.423	0.439	0.650	0.646	-0.07
30	0.531	0.541	0.684	0.713	0.716	0.39
31	0.844	0.854	0.919	0.390	0.393	0.03
32	-0.524	-0.540	-0.554	-1.051	-1.055	-0.07
33	0.491	0.484	0.592	0.747	0.745	0.58
34	0.956	1.019	1.157	0.579	0.602	1.08
35	-0.229	-0.178	0.134	-0.676	-0.657	-0.10
36	0.234	0.066	0.196	-0.060	-0.122	0.09
37	4.738	4.736	4.622	4.933	4.931	5.9
38	5.829	5.833	5.781	5.840	5.840	5.5
39	5.840	5.849	5.812	5.948	5.951	6.4
40	5.715	5.736	5.702	5.760	5.766	6.9
41	4.845	4.862	4.680	5.544	5.549	5.0
42	5.348	5.360	5.271	5.406	5.410	6.0
43	5.499	5.465	5.451	5.449	5.434	5.9
44	5.804	5.771	5.757	5.758	5.744	5.5
45	4.728	4.697	4.683	4.661	4.650	4.8
46	5.667	5.658	5.652	5.490	5.488	5.4
47	5.698	5.648	5.811	5.425	5.409	6.3
48	5.115	5.106	5.107	4.925	4.925	4.7
49	6.608	6.653	6.759	6.331	6.349	5.7
50	6.695	6.728	6.823	6.318	6.332	6.9
51	6.456	6.457	6.406	6.079	6.081	5.7
PA = Predicted activity derived from various QSAR model equations						

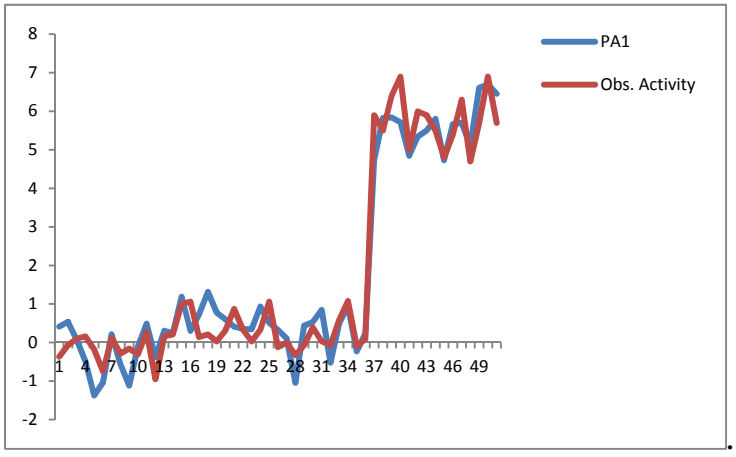
Several QSAR models in different combination of descriptors have been tried; the models chosen best five selected equations are those whose correlation coefficients values are above 0.90. The descriptors used in these models are presented in Table-10 and the QSAR model equations after the table numbered as 1, 2, 3, 4 and 5 and their graphs (1-5), respectively.

Table 10: Values of cross validation and correlation coefficients of best 5 QSAR models

PAE	rCV^2	r^2	Variable Counts	Descriptors used in QSAR models
PA1	0.907429	0.954382	7	Conformation Minimum Energy, HOMO Energy, Molecular Weight, SASA, Molar Volume, Parachor, Molar Refractivity
PA2	0.932422	0.9542	6	Conformation Minimum Energy, Molecular Weight, SASA, Molar Volume, Parachor, Molar Refractivity
PA3	0.924437	0.952831	6	Conformation Minimum Energy, Molecular Weight, Molar Volume, Parachor, Molar Refractivity, LogP
PA4	0.901121	0.942829	7	Conformational Minimum Energy, HOMO Energy, SASA, Molar Volume, Parachor, Molar Refractivity, LogP
PA5	0.918851	0.942804	6	Conformation Minimum Energy, SASA, Molar Volume, Parachor, Molar Refractivity, LogP
PAE = Predicted activity equations, rCV^2 = Cross validation coefficient, r^2 = Correlation coefficient				

QSAR Model Equation-1

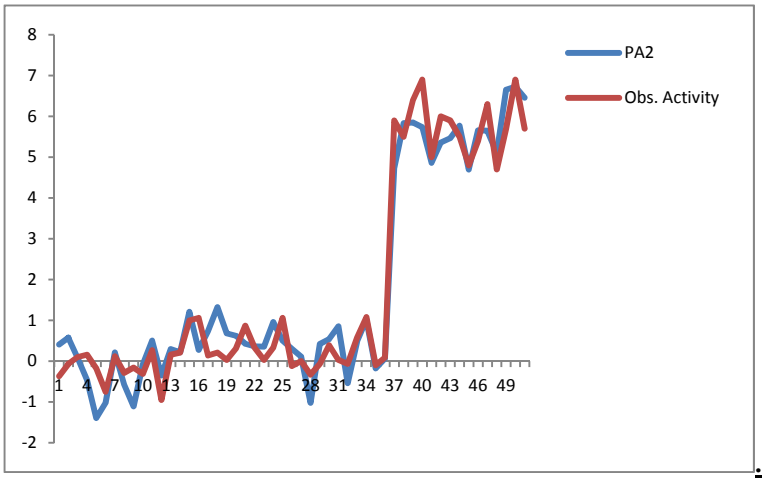
PA1 = 0.012117*ε+0.119786*ε_{HOMO}+0.0402073*Mw+0.018196*SASA+0.0827901*MV-0.0697818*Pc+0.130703 *MR+3.45723
rCV^2 = 0.907429
r^2 = 0.954382



Graph 1. Correlation between observed activity and predicted activity derived from regression model equation PA1

QSAR Model Equation-2

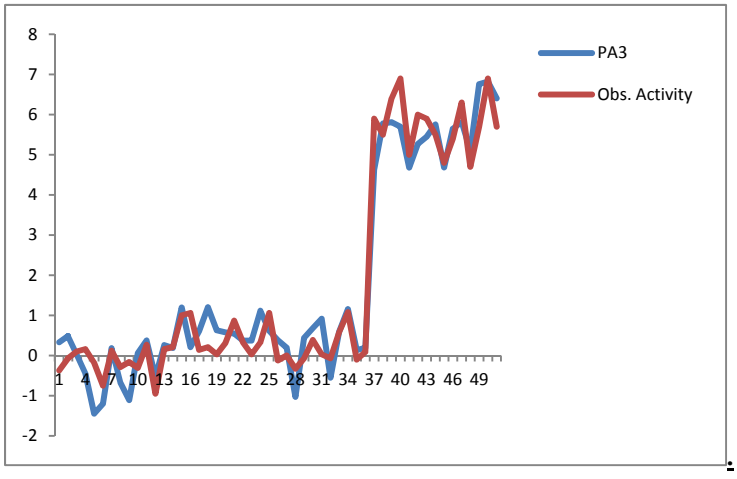
PA2 = 0.0125427*ε+0.0400518*Mw+0.0182581*SASA+0.0818386*MV-0.0693517*Pc+0.132491*MR+2.25093
rCV^2 = 0.932422
r^2 = 0.9542



Graph 2. Correlation between observed activity and predicted activity derived from regression model equation PA2

QSAR Model Equation-3

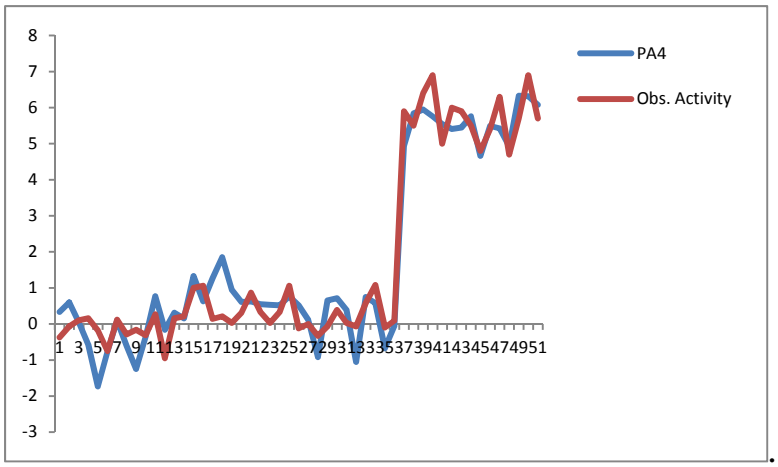
PA3 = 0.0122406*ε+0.047852*Mw+0.0881546*MV-0.0723991*Pc+ 0.134773*MR+0.0292349*LP+2.59905
rCV^2 = 0.924437
r^2 = 0.952831



Graph 3. Correlation between observed activity and predicted activity derived from regression model equation PA3

QSAR Model Equation-4

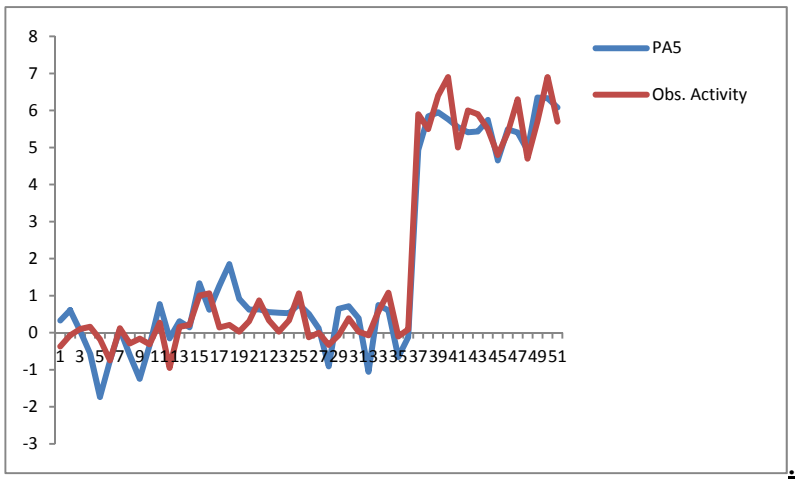
PA4 = 0.0137597*ε+0.0446904*ε_{HOMO}+0.0394608*SASA+0.0564635*MV-0.0478972*Pc+0.160674*MR-0.22895 *LP+2.41862
rCV^2 = 0.901121
r^2 = 0.942829



Graph 4. Correlation between observed activity and predicted activity derived from regression model equation PA4

QSAR Model Equation-5

PA5 = 0.0139207*ε+0.0393733*SASA+0.0561855*MV-0.0477665*Pc+0.161365*MR-0.23061*LP+1.96852
rCV^2 = 0.918851
r^2 = 0.942804



Graph 5. Correlation between observed activity and predicted activity derived from regression model equation PA5

These equations contain various descriptors in different combinations and each descriptor has a positive or negative coefficient attached to it. These coefficients along with the value of descriptor have a significant role in deciding the overall biological activity of the molecule as discussed below.

Examination of selected equation shows that coefficients of each parameter play an important role in deriving the biological activity. From the point of view of potency or biological activity of the drug molecule in terms of -logIC_{50} values, the weight of a negative co-efficient is very significant because it contributes towards a decreased value of -logIC_{50}, meaning increased value of biological activity. So the parameters with a negative co-efficient are most important followed by parameters with low weight positive coefficients and lastly the parameters with high weight positive coefficients.

On the basis of values of these coefficients, the associated descriptors are arranged in a sequence pertaining to their contribution towards overall biological activity of the molecule, in following decreasing order of biological activity of anti-ulcer agents-

Parachor (Pc) and/or LogP (LP) > Conformation Minimum Energy (ε) > Solvent Accessibility Surface Area (SASA) > Molecular Weight (Mw) > Molar Volume (MV) > HOMO Energy (ε_{HOMO}) > Molar Refractivity (MR)

CONCLUSION

The QSAR models developed by us in this paper represent some of the easiest ways of determining the biological activity of anti-ulcer agents. All the models are highly predictive and provides excellent values for cross validation coefficient (rCV^2) and correlation coefficient (r^2). Study and analysis of these models reveal that negative coefficients of regression model are most significant followed by positive coefficients of low weight and finally positive coefficients of high weight. The whole intention behind this was to facilitate the designing of new anti-ulcer drugs by computational method.

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