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Antifungal and Antibacterial activities of Imidazolylpyrimidines derivatives and their QSAR Studies under Conventional and Microwave-assisted

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Abstract : Quantitative structure-activity relationship (QSAR) models of newly synthesized substituted diphenyl imidazolylpyrimidines were established by using the molecular descriptors ST, MV, X_{index} MR, TE, LUMO, Log P, V AR, AECC. The logarithm of zone of inhibition of micro-organisms i.e. *S.aureus, S.typhi, P.aurogenosa, K.Pneunlonae and C.albicans* strains are used as key properties to evaluate the QSAR models. The Predictive ability and accuracy of the model is determined by a cross validation method.
Keywords : imidazolylpyrimidines derivatives, QSAR studies , molecular descriptors, cross validation, microwave-assisted .

Introduction

Novel medicines are typically developed using a trial and error approach, which is time consuming and costly. The application of quantitative structure-activity relationship (QSAR) methodologies to this problem has potential to decrease substantially the time and effort required to discover new medicines or to improve current ones in terms of their efficacy. QSAR establishes the mathematical relationship between physical, chemical, biological or environmental activities of interest and measurable or computable parameters such as topological, physicochemical, stereo chemical or electronic indices[1-6].

In recent years, microwave irradiation using commercial domestic ovens has been rapidly increased for optimization and acceleration of organic synthesis under solvent free conditions[7-8]. It has been reported for the variety of reactions such synthesis of heterocyclic and more recently for synthesis of polymers because of advantages such as reduction in reaction time, improved energy utilization, potential for lower processing temperature and improved product uniformity.

In connection with our interest in the use of microwave, we report herein the synthesis of several imidazolylpyrimidines in minimum solvent and minimum time under microwave irradiation (Scheme-I).

Candida albicans is the most prevalent opportunistic fungal pathogen in human that causes various forms of candidiasis ranging from superficial mucosal infection to life threatening systemic diseases in immunocompromised patients[9]. Many azoles inhibiting 14 α-lanosterol demcthylase in ergosterol biosynthesis pathway are known to exhibit interesting antibacterial activity and antifungal activities. However, reported drug class having azoles ring system[10] suffers major shortcomings i.e. a rapid development of resistance against *Candida albieans*. This has highlighted the need to discover new effective Antibiotic with new modes of action against both bacteria and fungi.

The present study aims at determining the antifungal and antibacterial activities of newly synthesized imidazolylpyrimidine derivatives by means of QSAR approach. During the programmed study on the development of green approach towards the synthesis of new organic molecules, a simple strategy for the synthesis of 4,5-diphenyl imidazolyl pyrimidine derivatives (3a-g) was designed, in which the two aryl rings were located at C-4 and C-5 on the opposite faces of the newly planar imidazole ring[11].

C.albicans with Griesofulvin. Since the synthesized compounds showed remarkable antifungal and antibacterial activity, we established QSAR analysis using ST, MV, X_{index}, MR, TE, LUMO, LogP, V AR, and AECC as appropriate molecular descriptors. After selecting these indices adequately, a very specific characterization of each chemical compound in QSAR models (Table 1.1) was obtained.

Descriptors Used: Before the calculation of the descriptors, the structures were fully, optimized using ACD chern. Sketch 10.3 software[12] and Chemdraw 3D Ultra 8.0.[13] All the descriptors used are calculated from the hydrogen suppressed molecular graphs. These molecular, graphs are obtained by deleting all the carbon - hydrogen as well as heteroatom - hydrogen bonds from the molecular structures of the imidazolepyrimidine derivatives. Dragon 5.4 (2006)[14] software was used for further calculations. The details of the calculations of these descriptors are available in the literature and therefore, they are not mentioned here.

Statistical analysis: The regression analysis is made using. maximum R2 method using MYSTAT 12[15] and Origin 5.0[16] software.

Experimental

All solvents were distilled prior to use. TLC was performed on silica gel G. Melting points were determined by open capillary method and are not correct. ^{1}HNMR and ^{13}CNMR spectra were recorded from $CDCl_3$/DMSO-d6 solution on a Brucker Avance-II 400(400 MHz) NMR Spectrometer. Chemical shifts are reported in ppm using TMS as an internal, standard. IR spectra were obtained on a Shimadzu FTIR spectrophotometer, using KBr discs. Mass spectra were recorded by using Shimadzu gas chromatograph coupled with QP5050 Spectrometer at 1-1.5 ev.

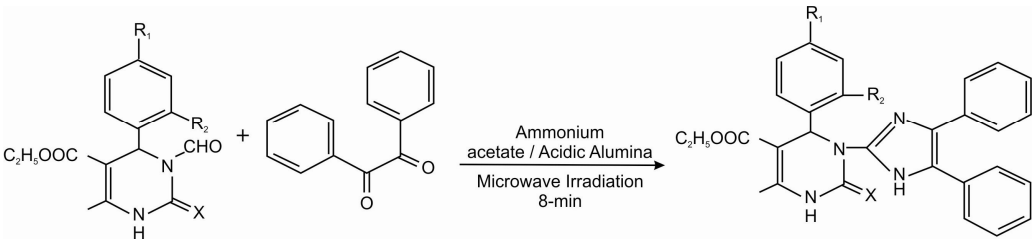
General procedure for synthesis of substituted ethyl 1, 2, 3, 6-tetrahydro-4-methyl-2-oxo/thioxo-6-phenyl-1- (4, 5-diphenyl-1-H-imidazol-2-yl) pyrimidine-5-carboxylate (3a-g)

Method-A (Conventional) :

Benzil (2.5m mole; 5.25g), ethyl-1-formyl-1,,2,3,6-tetrahydro-4-methy-6-phenyl-2-oxo-pyrimidine-5-carboxylate (2.5m Mole; 11.95g) and ammonium acetate (0.12 mole; 10g) were dissolved in glacial acetic acid. The reaction mixture was refluxed for 10-12 hours. It was then cooled and poured in cold water then the precipitate was formed, filtered, washed with ammonium hydroxide and dried. The product was recrystallization from ethanol.**Yield :** 64% **M.P.** 160ºC.

Method-B (Microwave Irradiation)

Benzil (2.5m mole; 5.25g), ethyl-1-formyl-1,,2,3,6-tetrahydro-4-methy-6-phenyl-2-thioxopyrimidine-5-carboxylate (2.5m Mole; 11.95g) and ammonium acetate (0.12 mole; 10g) were dissolved in glacial acetic acid. The contents were thoroughly mixed. The reaction mixture was subjected to microwave irradiation in a commercially available IFB domestic microwave oven having a maximum power output of 110w operating at 2450 MHz intermittently at 30 sec. intervals for 8 min. on completion of reaction as monitored by TLC, the product was diluted with water then the precipitate was formed, filtered, washed with ammonium hydroxide and dried. The product was recrystallization from ethanol. The purity of the compounds was checked with TLC. **Yield :** 79% **M.P.** 160ºC.



(Scheme 1)

Result and Discussion

Substituted ethyl 1, 2, 3, 6-tetrahydro-4-methyl-2-oxo/thioxo-6-phenyl-l- (4, 5-diphenylI-H-imidazol-2-yl) pyrimidine-5-carboxylates (3a-g) were synthesized by condensing substituted ethyl-1-formyl-l, 2, 3, 6-tetrahydro-4-methyl-6-phenyl-2-oxo/thioxopyrimidine-5-carboxylates (la-g) and Benzil with ammonium acetate by using acidic alumina, and four drops of glacial acetic acid under solvent free microwave irradiation for 8 minutes and conventional method for 12 hours. (Scheme 1)

The QSAR study of newly synthesized ethyl-1, 2, 3, 6-tetrahydro-4-methyl-2-oxo/thioxo6-phenyl-l-(4,5-diphenyl-lH-imidazol-2-yl) pyrimidine-5-carboxylate derivatives (3a-g) is not reported in the literature. Hence the synthesized compounds were tested against S.aureus, S.typhi, P.aurogenosa, K.pneumonae in comparison with Norfloxacin.

The structure of ethyl 1, 2, 3, 6-tetrahydro-4:"methyl-2-oxo-6-phenyl-1- (4, 5-diphenyl-lH-imidazol-2-yl) pyrimidine-5-carboxylate (3a) was supported by IR, IHNMR, 13_{CNMR}, MASS spectral data. IR spectra exhibited the N-H absorption band at 3198cm-^{1}, ester carbonyl group at 1750cm-^{1}, C=C stretch at 1495 em-I, C=N stretch at 1435cm-^{1} were observed. IHNMR of (3a) in ($CDC1_3$/$DMSOd_6$) was nicely resolved and showed the appearance of N-H proton as a characteristic singlet at 8 8.9 and the aromatic protons as a multiplet at 8 7.1-7.9 (Table 1.2).

Table 1.1:Physical Characteristic data of the compound synthesized (3a-g)

Compound	X	R_1	R_2	Method-A Yield/Time %/hr	Method-B Yield/Time %/min	MP(0C)	Mol.Formula
3a	O	H	U	64/12	79/8	160	$C_{29}H_{26}N_4O_3$
3b	O	H	NO2	64/12	78/8	210	$C_{29}H_{25}N_5O_5Cl$
3c	O	Cl	H	62/12	69/8	180	$C_{29}H_{25}N_4O_9Cl$
3d	O	OCH3	H	65/12	72/8	240	$C_{30}H_{28}N_4O_4$
3e	S	U	H	65/12	78/8	190	$C_{29}H_{26}N_4O_2S$
3f	S	Cl	H	63/12	75/8	195	$C_{29}H_{25}N_4O_2SCl$
3g	S	H	NO2	60/12	67/8	220	$C_{29}H_{25}N_5O_4S$

Table 1.2: Characteristic spectral data compound synthesized (3a-g)

Compund	IR (KBr disc) cm^{-1}	^{1}HNMR (DMSO/d6) □, ppm	^{13}CNMR	MASS
3a	3198 (N-H), 1499 (C=C), 1435 (C=N)	1.1 (t,3H,CH_3, *J*=8), 2.3 (s,3H,CH_3), 4.2 (q, 2H, CH_2, *J*=4.8), 5.1 (s,1H,Ar-H), 8.9 (s,1H,N-H)	13.7, 17.7, 54.4, 59.0, 99.7, 127.2, 128.6, 129.5, 129.3, 132.7, 147.1, 184.2, 158.8, 165.3, 167.1, 194.1	478
3b	3190 (N-H)1493 (C=C), 1430 (C=N)	1.3 (t,3H,CH_3, *J*=8), 2.1 (s,3H,CH_3), 4.1 (q, 2H, CH_2, *J*=4.8), 5.4 (s,1H,Ar-H), 8.7 (s,1H,N-H)	13.5, 17.9, 54.2, 59.0, 99.6, 127.1, 128.6, 129.5, 129.3, 132.3, 134.0, 147.8, 148.5, 158.8, 165.7, 167.1, 194.3	523
3c	3198 (N-H) 1549 (C=C), 1435(C=N)	1.4 (t,3H,CH_3, *J*=7.6), 2.4 (s,3H,CH_3), 4.0 (q, 2H, CH_2, *J*=4.2), 5.2 (s,1H,Ar-H), 9.2 (s,1H,N-H)	13.4, 17.6, 54.3, 59.2, 99.7, 127.2, 128.4, 129.5, 129.6, 132.7, 134.6, 147.1, 184.2, 158.53, 167.1, 194.8	512
3d	3195 (N-H)1489 (C=C), 1469 (C=N)	1.1 (t,3H,CH_3, *J*=8.2), 2.3 (s,3H,CH_3), 3.7 (s, 3H, OCH_3) 4.0 (q, 2H, CH_2, *J*=4.8), 5.3 (s,1H,Ar-H), 8.9 (s,1H,N-H)	13.2, 17.6, 54.1, 59.3, 99.7, 127.2, 128.6, 129.5, 129.3, 132.7, 134.1, 147.1, 148.2, 158.8, 165.3, 167.1, 194.5	508
3e	3198 (N-H)1494 (C=C), 1430 (C=N)	1.3 (t,3H,CH_3, *J*=8), 2.2 (s,3H,CH_3), 4.2 (q, 2H, CH_2, *J*=4.8), 5.5 (s,1H,Ar-H), 9.5 (s,1H,N-H)	13.3, 17.7, 54.4, 59.0, 99.2, 127.4, 128.6, 129.5, 129.3, 132.7, 134.2, 147.1, 148.2, 158.8, 165.3, 167.1, 194.3	494
3f	3200 (N-H)1493 (C=C), 1433 (C=N)	1.2 (t,3H,CH_3, *J*=8), 2.4 (s,3H,CH_3), 4.1 (q, 2H, CH_2, *J*=4.8), 5.3 (s,1H,Ar-H), 9.3 (s,1H,N-H)	13.7, 17.7, 54.4, 59.3, 99.7, 127.2, 128.6, 129.5, 129.3, 132.7, 134.0, 147.1, 148.2, 158.8, 165.3, 167.1, 194.4	528
3g	3205 (N-H)1495 (C=C), 1435 (C=N)	1.3 (t,3H,CH_3, *J*=8), 2.3 (s,3H,CH_3), 4.0 (q, 2H, CH_2, *J*=4.6), 5.1 (s,1H,Ar-H), 9.6 (s,1H,N-H)	13.4, 17.6, 54.4, 59.0, 99.3, 127.2, 128.6, 129.5, 129.3, 132.7, 134.0, 147.1, 148.2, 158.8, 165.3, 167.1, 194.7	539

The appearance of multip1ets of 14 protons at 8 7.2-8.5 confirmed the presence of two more phenyl rings attached to the basic moiety .The disappearance of the -CHO peak at 8 10.2-10.4 supported the formation of product 3a. ^{13}CNMR showed the disappearance of peak of H-C=O in compound 3a and the appearance of peak of N-C-N at 8 134.0 which confirmed its structure.

Antifungal activity

The antifungal activities of compounds (3 a-g) have been assayed in vitro at a concentration 100□g disc-[1] against *C.albicans*. Griesofulvin was used as standard fungicide for the antifungal test. Muller-Hinton agar was used as basal medium for test fungi. Glass Petri dishes were sterilized and 10ml of sterilized melted MH agar medium (4S°C) was poured into each Petri dish. After solidification of the medium small portion of mycelium of *C.albicans* was spread carefully over the centre of each MH agar plate with the help of spreader. Thus fungus was transferred to each plate. The plates were then incubated at (27°C) and after half an hour of incubation they were ready for use. The prepared discs of test sample were placed gently on the solidified agar plate, freshly seeded with the test organisms with sterile forceps. The plates were then incubated at 37.5ºC for 24hr. Dimethyl formamide (DMF) was used as a solvent to prepare desire solutions of the compounds initially[17-18].

The antifungal studies revealed that the compounds 3b and 3c having chloro and nitro groups respectively along with oxopyrimidine moiety were found to be most active amongst the entire tested compounds. 3a and 3g exhibited moderate activity in comparison with other compounds. 3f showed less activity where as 3d and 3e were found to be inactive against the *C.albicans* (Table 1.3).

Antibacterial Activity

The antibacterial activity of compounds (3a-g), which has been, assayed at concentration of 100□g disc[-1] against strains of gram +ve and gram -ve pathogenic bacteria *(S. typhi, Paltrogenosa, K Pneumonae and S.aureus)*. Initially, susceptibility testing was carried out by measuring the inhibitory zone diameter on Muller-Hinton agar with conventional paper disc diffusion method, the inhibitory zone diameter was recorded and rounded off to the nearest whole numbers (mm) for further QSAR analysis[17-18]. The sensitivity of compounds (3a-g) against these organisms is depicted in (Table 1.4). The results were compared with standard drug i.e. Norfloxacin.

The screening results revealed that in addition to (3a-c), the compound 3d were found to be the most active against S.aureus amongst all the tested compounds. S. typhi is highly sensitive to the compound 3b and (3e-g) and moderately sensitive to Compounds 3a and 3c. It has been observed that *P.aurogenosa and K. Pneumonae* are highly resistant to the synthesized compounds.

Table 1.3:Antimicrobial screening results of compound synthesized

Sr.No.	Compounds	Zone of inhibition in mm for conc. for 100□g/ml	Logarithm of zone of inhibition in mm
C.albicans			
1.	3a	9.0	2.197
2.	3b	12.0	2.485
3.	3c	13.0	2.565
4.	3f	6.0	1.791
5.	3g	9.0	2.197
K.pneumonae			
1.	3a	12.0	2.485
2.	3b	12.0	2.485
3.	3c	10.0	2.303
4.	3d	15.0	2.708
5.	3e	9.0	2.197
6.	3f	18.0	2.890
7.	3g	8.0	2.079
P.aurogenosa			
1.	3a	9.0	2.197
2.	3c	12.0	2.485
3.	3d	10.0	2.303
4.	3e	12.0	2.485
5.	3f	6.0	1.791
6.	3g	10.0	2.303
S.typhi			
1.	3a	9.0	2.197
2.	3b	12.0	2.485
3.	3c	9.0	2.197

4.	3e	13.0	2.565
5.	3f	11.0	2.398
6.	3g	13.0	2.565
S.aureus			
1.	3a	10.0	2.303
2.	3b	10.0	2.303
3.	3c	9.0	2.197
4.	3d	12.0	2.485
5.	3e	6.0	1.791
6.	3f	6.0	1.791
7.	3g	7.0	1.946

Table 1.4 : Physicochemical constants, topological and structural descriptors used in the present study.

Sr. No.	Description	Notation	Sr. No.	Description	Notation
1	Molecular Weight	MW	29	Mol. Walk Count of Order 03	MWC03
2	Number of Atoms	nAT	30	Total Walk Count	TWC
3	Number of Rings	nCIC	31	Randie ID Number	CID
4	Number of five member Ring	nR05	32	Balaban ID Number	BID
5	Number of six member Ring	nR06	33	Randic Connectivity Index Chi-0	X0
6	All path Wiener Index	Wap	34	Randic Connectivity Index Chi-1	X1
7	Pogliani Number	Dz	35	Randic Connectivity Index Chi-2	X2
8	Polarity Number	Pol	37	Randic Connectivity Index Chi-3	X3
9	Means Square Distance Index (Balaban)	MSD	38	Solvation Connectivity Index Chi-0	X0Sol
10	Schultz Mol. Topological Index	SMTI	39	Solvation Connectivity Index Chi-1	X1Sol
11	Gutman Mol. Topological Index	GMTI	40	Solvation Connectivity Index Chi-2	X2Sol
12	Xu Index	Xu	41	Randic Mod	X_{MOD}
13	Wiener Index	W	42	Balaban U Index	U_{index}
14	Mean Wiener Index	WA	43	Balaban V Index	V_{index}
15	Quasi Wiener Index	QW	45	Balaban X Index	X_{index}
16	Balaban Distribution connectivity index	J	46	Balaban Y Index	Y_{index}
17	Kier flexibility index	PHI	47	Eigen value sum from Vander waals weighted distance matrix	SEigv
18	Path/walk2-Randic Shape Index	PW2	48	Eigen value sum from electonegativity matrix	SEige
19	Path/walk3-Randic Shape Index	PW3	49	Molar Refractivity	MR
20	Eccentric Connectivity Index	CSI	50	Molar Volume	MV
21	Eccentricity	ECC	51	Surface Tension	ST
22	Average Eccentricity	AECC	52	Density	Density
23	Eccentric	DECC	53	Polarizability	Polarizability

24	Unipolarity	UNIP	54	Partition Coefficient	LogP
25	Variation	VAR	55	Total Energy	TE
26	Balaban Centric Index	BAC	56	HOMO Energy	HOMO
27	Mol. Walk Count of Order 01	MWC01	57	LUMO Energy	LUMO
28	Mol. Walk Count of Order 02	MWC02			

Table 1.5: The calculated values of descriptors ST, MV, X;,d", MR, TE, LUMO, LogP, V AR, and AECC are summarized.

Sr.No.	Compound	VAR	X_{index}	V_{index}	MV	MR	ST	LogP	TE	LUMO	AECC
1	3a	146	0.288	0.191	238.9	135.97	52.3	4.5456	2305.6	-0.502	10.279
2	3b	152	0.29	0.193	372.8	139.98	54.9	4.3552	2882.4	-0.874	10.342
3	3c	146	0.288	0.191	379.3	136.23	52.3	4.7657	2305.04	-0.635	10.278
4	3d	175	0.285	0.188	391.4	138.02	52.0	4.0811	2299.28	-0.554	10.838
5	3e	129	0.291	0.193	351.0	138.9	75.3	5.7991	2310.25	-1.08	9.714
6	3f	146	0.288	0.191	361.8	143.73	76.8	6.3573	2309.97	-1.195	10.278
7	3g	152	0.29	0.193	384.2	146.45	53.2	5.9468	2905.37	-1.009	10.342

QSAR Study

In the present study authors tried to develop best QSAR model for each microorganisms to explain the correlation between the physicochemical parameters and antimicrobial activity of diphenyl imidazolyl pyrimidines (DPIP) derivatives against 5 different microorganisms. The details of molecular structures of (DPIP) derivatives used in the present study are illustrated in (Table 1.1). The antifungal and

antibacterial activities of above said compounds against *S. aureus,* S. *typhi, Paurogenosa, K.pneumonae, and Calbicans* are depicted in (Table 1.3). Here, we have used logarithm of activities to be studied. In order to model and predict the specific activity, 57 physicochemical constants, topological and structural descriptors (Table 1.4) were considered as possible input candidates to the model[13].

A persual of (Table 1.3) showed that 3-a, b, c, f, g; these 5 compounds are effective against *C.albicans* while all are effective in case *of K.pnellmonae and* S. *allrells. P.allrogenosa,* S. *typhi* are found to be resistant against 3b and 3d. In obtaining QSAR models, we have used logarithm of zone of inhibition to account for their antifungal and antibacteriai activities against the five microbes mentioned earlier. Based on the activity values we observed, we can propose the following order of antimicrobial activity.

Against *Calbicans*

3c>3b>3a=3g>3f (1)

Against *K.pneumonae*

3f>3d>3a=3b>3c>3e>3g (2)

Against *Paurogenosa*

3c=3e>3d=3g>3a>3f (3)

Against S. *typhi*

3e=3g>3b>3f>3a=3c (4)

Against S. *aureus*

3d>3a=3b>3c>3g>3e=3f (5)

Table 1.6 : Correlation matrices for the DPIP used

	Activity	VAR	X_{index}	V_{index}	MV	MR	ST	LogP	TE	LUMO	AECC
Calbicans n = 5											
Activity	1.000										
VAR	0.282	1.000									
X_{index}	0.282	1.000	1.000								
V_{index}	0.282	1.000	1.000	1.000							
MV	0.512	0.204	0.204	0.204	1.000						
MR	-0.54	0.544	0.544	0.544	-0.26	1.000					
ST	-0.819	-0.33	-0.331	-0.331	-0.90	0.429	1.000				
LogP	-0.797	-0.04	-0.044	-0.044	-0.42	0.812	0.708	1.000			
TE	0.268	1.000	1.000	1.000	0.210	0.56	-0.33	-0.02	1.000		
LUMO	0.619	-0.32	-0.323	-0.323	0.679	-0.88	-0.75	-0.82	-0.33	1.000	
AECC	0.282	1.000	1.000	1.000	0.204	0.544	-0.33	-0.04	1.000	-0.323	1.000
K.pneumonae n = 7											
Activity	1.000										
VAR	0.419	1.000									
X_{index}	-0.649	-0.78	1.000								
V_{index}	-0.63	-0.72	0.984	1.000							
MV	0.028	0.798	-0.632	-0.538	1.000						
MR	-0.086	0.007	0.342	0.399	-0.14	1.000					
ST	0.241	-0.59	0.355	0.261	-0.91	0.293	1.000				
LogP	-0.129	0.56	0.494	0.473	-0.62	0.714	0.739	1.000			
TE	-0.414	0.117	0.500	0.601	0.167	0.597	-0.32	0.044	1.000		
LUMO	0.046	0.491	-0.612	-0.589	0.751	-0.76	-0.79	-0.87	-0.28	1.000	
AECC	0.477	0.979	-0.82	-0.735	0.836	-0.01	-0.62	-0.55	0.086	0.525	1.000
P.aurogenosa n = 6											
Activity	1.000										
VAR	-0.122	1.000									
X_{index}	0.238	-0.86	1.000								
V_{index}	0.173	-0.82	0.985	1.000							
MV	0.116	0.808	-0.646	-0.556	1.000						
MR	-0.438	0.007	0.358	0.428	-0.15	1.000					
ST	-0.404	-0.59	0.442	0.363	-0.94	0.300	1.000				
LogP	-0.413	-0.58	0.699	0.721	-0.69	0.775	0.737	1.000			
TE	0.076	0.084	0.408	0.502	0.268	0.759	-0.27	0.391	1.000		
LUMO	0.37	0.499	-0.626	-0.613	0.75	-0.76	-0.82	-0.97	-0.31	1.000	
AECC	-0.219	0.979	-0.887	-0.823	0.843	-0.01	-0.62	-0.57	0.060	0.531	1.000
S.typhi n = 6											
Activity	1.000										
VAR	-0.181	1.000									
X_{index}	0.875	-0.38	1.000								

V_{index}	0.885	-0.11	0.962	1.000							
MV	-0.465	0.774	-0.431	-0.233	1.000						
MR	0.694	0.331	0.292	0.412	-0.04	1.000					
ST	0.376	-0.67	0.181	-0.004	-0.90	0.247	1.000				
LogP	0.516	-0.29	0.168	0.094	-0.48	0.722	0.718	1.000			
TE	0.574	0.623	0.489	0.710	0.368	0.574	-0.43	-0.11	1.000		
LUMO	-0.79	0.233	-0.465	-0.430	0.678	-0.76	-0.77	-0.83	-0.18	1.000	
AECC	-0.372	0.975	-0.575	-0.328	0.788	0.222	-0.64	-0.29	0.432	0.319	1.000
S.aureus n=7											
Activity	1.000										
VAR	0.725	1.000									
X_{index}	-0.626	-0.78	1.000								
V_{index}	-0.577	-0.72	0.984	1.000							
MV	0.778	0.798	-0.632	-0.538	1.000						
MR	-0.583	0.007	0.342	0.399	-0.14	1.000					
ST	-0.817	-0.59	0.355	0.261	-0.91	0.293	1.000				
LogP	-0.968	-0.56	-0.494	0.473	-0.62	-0.71	0.739	1.000			
TE	--	0.117	0.500	0.601	0.167	0.597	-0.32	0.044	1.000		
LUMO	0.887	0.491	-0.612	-0.589	0.751	-0.76	-0.79	-0.87	-0.28	1.000	
AECC	0.728	0.979	-0.82	-0.735	0.836	-0.01	-0.62	-0.55	0.086	0.525	1.000

It is interesting to record that compound 3c shows maximum zone of inhibition against *C.albicans and P.aurogenosa* but showed moderate zone of inhibition against *K.pneumonae and* S. *aureus* and minimum zone of inhibition against S.*typhi.* Likewise compound 3f showed maximum zone of inhibition against *K.pneumonae* and minimum zone of inhibition against all other strains used. Furthennore, these sequences (order) do not establish any quantitative structure-activity relationship (QSAR). Therefore, we have made such study using above said descriptors, which encodes the molecular structures of DPIP numerically. Since, different compounds are found effective against five microorganisms used, we have obtained 5 different correlation matrices (Table 1.6) for preliminary investigations of correlation among descriptors against the antifungal and antibacterial activities. Based on the microorganisms used, our discussion has been divided into five different segments.

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