3d-Qsar Studies for Some Schiff Bases against Fungal Pathogen

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Abstract: *3D QSAR viz. 3 descriptor quantitative structure and activity relationship studies for a series of compounds i.e. Schiff base derivatives using their semi-empirical quantum chemical descriptors and their laboratory reported activities against pathogen viz. .Colletotrichumfalcatum (ITCC 6656) have been carried out and reported in the present paper. Graphs between observed and predicted activities, both in the terms of p(MIC)cal and p(MIC) obs. are also being reported on the basis of which this may be concluded that some parameters/descriptors have positive contribution towards the activity. The method has been proved to be useful tool for such type of studies.*

Key words: *Semiempirical/3D-qsar/fungal pathogen/Schiff bases compounds*

I.   Introduction

The battle against the infectious diseases has become a never ending process, as micro-organisms are becoming resistant more quickly than new drugs are being made available. Keeping this view, medicinal chemists are also trying out their best to speed up the drug discovery process for finding the lead molecule by using different techniques which includes QSAR (Quantitative Structure and Activity Relationship), CADD (Computer Aided Drug Design), Molecular Modeling, Combinatorial Chemistry and Microwave assisted synthesis. The use of these techniques has reduced the time required for primary screening of the molecule to locate the lead molecule.

Previously the studies involve the checking of antimicrobial activities of naturally occurring and /or synthesized compounds in the laboratory which may include organic compounds and inorganic complexes which were the areas of interest of many workers for so many years.

QSAR (Quantitative Structure and Activity Relationship) technique has been developed as a recent and finest technique in the field of drug designing. This technique has its foundation on the statistical analysis particular regression analysis of structural descriptors of compounds under studies with their lab. reported activities. In some of the recent references scientists have even utilized electronic properties or parameters of compounds/ drugs computed on the basis of Quantum Chemical Calculation viz. ab initio or semi-empirical studies as descriptors for QSAR studies and correlated these descriptors with activities of the compounds against a certain microorganism, which has been proved as a step ahead in the related field.

Schiff bases are the class of compounds in which an aldehyde and an amine condensed to form azomethinic linkage to yield a Schiff base. Schiff bases are of interest of many workers for so many years in the field of synthetic organic chemistry as well as in the synthesis and studies of complexes also. A lot of references including metal complexes with Schiff bases are known. Scientists are also trying to locate and study the antimicrobial activities of Schiff bases as well as of their metal complexes against various pathogens.

Literature survey carried out in the proposed field (1-32) revealed that on the workers/ scientists have tried many naturally occurring and synthetic compounds to check their activities against various microorganisms. QSAR studies of various series of compounds have also been carried out successfully. Some of the workers have also tried to correlate activities with 2 descriptors and 3 descriptors of the compounds pertaining to 2D- QSAR and 3D- QSAR studies(1-32).

Keeping above discussion in mind, in this present paper QSAR precisely 3D-QSAR studies which have been carried out on a new series of compounds i.e. Schiff base derivatives compounds shown in figure) with their activities against .   Colletotrichumfalcatum (ITCC 6656) are reported.

II.   Experimental

Preparation of Schiff bases:-

Schiff base compounds under study were synthesized by treating the appropriate amine (~1.0 mmol) with corresponding aldehyde (~1.1mmol) in appropriate solvents such as ethyl alcohol and the reaction mixtures were refluxed for 6 to 12 hours using water condenser. In some cases products were obtained after cooling the reaction mixture as such while in some cases products were obtained after cooling it on ice bath. Schiff bases obtained were then filtered and re-crystallized using appropriate solvents i.e. either alcohol or ether (yield of the Schiff base compounds ~60- 70 %.)
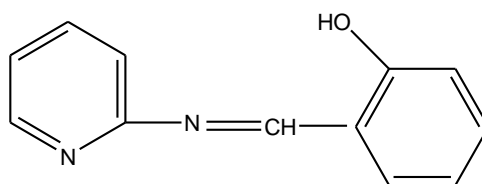
Compounds viz. Schiff bases (SB1-SB15) which are under study are shown in the figure -1. Analytical studies were also carried out for the synthesized compounds. These are given in the tables 1along with their melting points.
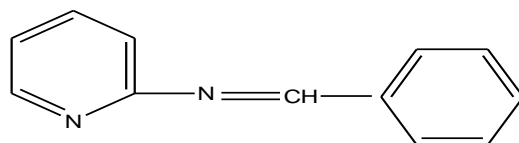
2N – [Benzalidene] Aminopyridine (SB-1)
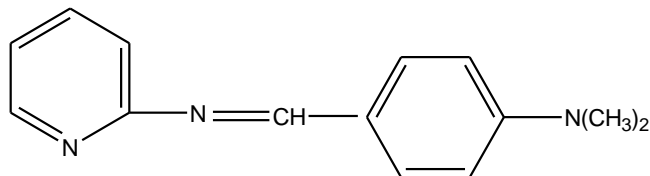
2N – [p-Dimethylaminobenzalidene] aminopyridine (SB-2)

2N – [2-Hydroxybenzalidene] aminopyridine (SB-3)

2N – [3,4,5-Trimethoxybenzalidene] aminopyridine (SB-4)

2N – [Furfuralidene] aminopyridine (SB-5)

3N – [Furfuralidene] aminopyridine (SB-6)

3N – [Benzalidene] aminopyridine (SB-7)

3N – [p-Dimethylaminobenzalidene] aminopyridine (SB-8)

3N – [2-Hydroxybenzalidene] aminopyridine (SB-9)

3N – [3,4,5-Trimethoxybenzalidene] aminopyridine (SB-10)
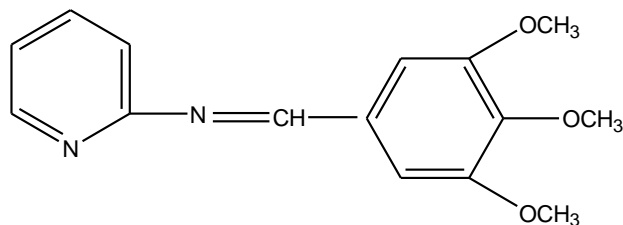
4N – [Furfuralidene] aminopyridine (SB-11)

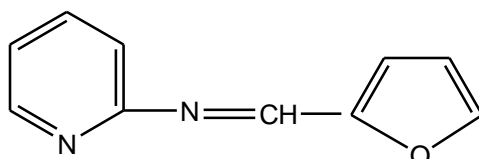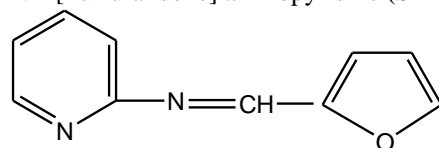4N – [Benzalidene] aminopyridine (SB-12)

4N – [p-Dimethylaminobenzalidene] aminopyridine (SB-13)
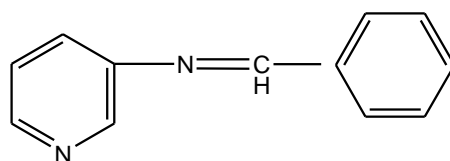
4N – [2-hydroxybenzalidene] aminopyridine (SB-14)

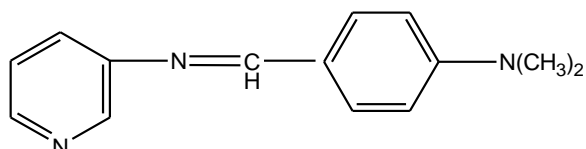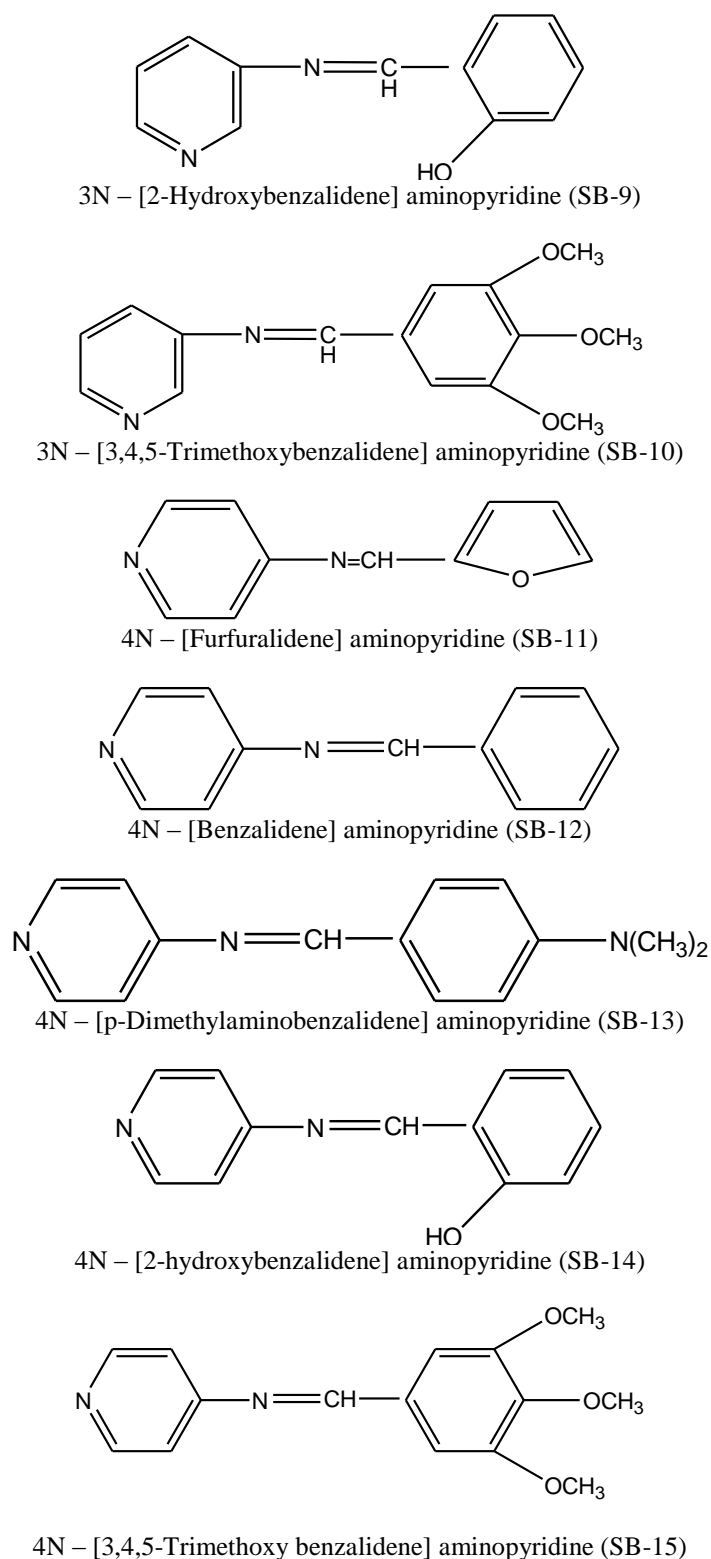4N – [3,4,5-Trimethoxy benzalidene] aminopyridine (SB-15)

Figure-1: Schiff Base Compounds Under Study

Table 1: - Analytical studies for the Schiff bases under study

Compound	M. Pt. (^{0}C)	C Found (Calcd.)	H Found (Calcd.)	N Found (Calcd.)
SB-1	180-185	76.26 (79.3%)	5.85 (5.4%)	18.28 (15.3%)
SB-2	185-190	76.76 (74.6%)	5.67 (6.66%)	15.34 (18.6%)
SB-3	190-192	70.9 (72.0%)	6.65 (5.0%)	13.05 (14.0%)
SB-4	182-185	64.69 (64.6%)	6.004 (6.1%)	7.41 (10.7%)
SB-5	168-172	67.46 (69.7%)	4.76 (4.6%)	14.86 (16.2%)
SB-6	172-175	67.64 (69.7%)	4.67 (4.6%)	14.96 (16.2%)
SB-7	182-189	77.62 (79.3%)	5.05 (5.4%)	17.82 (15.3%)
SB-8	188-192	79.67 (74.6%)	7.67 (6.66%)	16.89 (18.6%)
SB-9	175-180	70.91 (72.0%)	6.67 (5.0%)	13.50 (14.0%)
SB-10	185-189	64.96 (64.6%)	6.40 (6.1%)	7.42 (10.7%)
SB-11	170-174	64.56 (69.7%)	6.00 (4.6%)	14.20 (16.2%)
SB-12	183-188	76.82 (79.3%)	5.80 (5.4%)	18.80 (15.3%)
SB-13	187-190	78.67 (74.6%)	7.77 (6.66%)	16.98 (18.6%)
SB-14	176-181	70.9 (72.0%)	6.66 (5.0%)	12.4 (14.0%)
SB-15	183-186	66.08 (64.6%)	6.115 (6.1%)	7.813 (10.7%)

These compounds were also established on the basis of modern spectroscopic studies viz. i.r. spectral studies. N.M.R. spectral and Mass spectral studies for some of the representative compounds were also carried out.Analysis of the studies is given below:-

I.R. spectral studies:-
Assignments of peaks are given in the table-2 for Schiff base compounds. I.R spectral analysis show that (C=N) stretching azomethine peaks are predominant in the spectra of every Schiff base compound. This peak appears ca 1635-1590 cm^{-1} in the spectra of compounds under study. Apart from these peaks ring stretching peaks, N- phenyl stretching peak, ring breathing of benzene, C-N-C bending, C-H out of plane deformation of mono substituted benzene and Out of plane bending of mono substituted benzene are also reported in the table-2.

NMR spectral studies:-
NMR spectral studies are of less interest for the compounds under study. However, these spectra were also recorded for some representative compounds on NMR spectrometer Bruker DRX-300 with due acknowledgement to C.D.R.I. Lucknow. Some notable peaks in these spectra are listed below:-

SB1: 1.062(s);1.220 (s); 2.118-2.065 (d); 2.490 (s); 3.021(s); 3.341(s); 5.833 (s); 6.161(s); 6.458-6.393 (t); 6.584- 6.520 (t); 6.680-6.636(t); 7.227-7.206 (d); 7.302-7.278 (d); 7.376-7.353 (d); 7.464-7.736 (d); 7.534-7.509 (d); 7.665- 7.585 (q); 7.828- 7.687 (q).

SB3:- 2.260 (s); 2.490 (s); 2.997 (s); 3.326 (s); 6.179-6.159 (d); 6.205(s0; 6.572-6.460 (d); 6.731- 6.599 (q); 6.925 (s); 6.991-6.971 (d); 7.100-7.073 (d);7.338-7.282 (t);7.463- 7.442 (d); 7.668-7.486(t); 7.919(s); 9.776 (s); 10.250(s); 10.695 (s) ppm respectively.

MASS spectral studies:-
Mass spectral studies of some representative Schiff base compounds have been carried out. Notable peaks in different compounds are:- base peaks at SB-1 :-228, SB-3 :-154, SB-4:- 273, SB-5: -173, with parent ion peaks at SB-1 :-181, SB-3 :-199, SB-4:- 273, SB-5: -173,. These parent peaks confirm the mol. weights of the compounds under study. Mass spectral analyses of the compounds are given in tables 3-6.

Table-2: - IR spectral analysis for the Schiff base compounds under study

Assignment/ Compound	(C=N) Stretching azomethine	Ring stret-ching	N-Phenyl stret-ching	☐(C-N)	Ring breathing of benzene	C-N-C Ben-ding	C-H out of plane deformation of mono substituted benzene	Out of plane bending of mono substituted benzene
SB-1	1600.1s	1515.8m 1457.4s 1434.4s	1396.3w 1320.5m	1151.2m	1088m 988m	925w 857w 813w	767m 695m	534m
SB-2	1597s	1530w 1488w 1438w	1370m 1312m	1165m	1065w 991w	937w 815m	725w 695w	511w
SB-3	1608s	1552m 1496m 1428m	1400w 1353w	1185s	1145m 993m	913m 845m	754m 695sh	527w
SB-4	1591s	1555sh 1503m 1421m	1391m 1330s	1186s	1127s 989m	915w	771w 677w	523w
SB-5	1600s	1569w 1482m 1439m	1392w 1313m	1150w	1125sh 988w	925w	771m 695sh	553w
SB-6	1624s	1583s 1525m 1482s	1390sh 1293m	1186w	1131w 990sh	925w	797m 705m	550w
SB-7	1635s	1583w 1482w 1420w	1294w	1187m	1132m	883s	798m 706m	550w
SB-8	1599s	1551m 1527w 1437w	1398m 1330w	1169s	1124w 1064w	942w	817m 708m	516m
SB-9	1595s	1535w 1480w 1438w	1375m 1312w	1160m	1060w 991w	935w 815m	725w 695w	515w
SB-10	1624s	1583s 1539s 1502s	1372m 1329s	1186s	1126s 1041s	950w	842w 710m	515w
SB-11	1600vs	1585sh 1513m 1423w	1372sh 1309m	1214s	1129m 1087m	933m	868w 816m	531m
SB-12	1605s	1510m 1455s 1434s	1395w 1325m	1150m	1088m 988m	925w 857w 813w	760m 690m	534m
SB-13	1600s	1585sh 1512m	1431w 1331w	1216w	1166w 1085sh	935sh	820m 725w	534w
SB-14	1604s	1527s 1510sh	1478w 1435w 1343m	1269w	1197m 1085sh	940sh	828w 760m	525w
SB-15	1590vs	1505s 1461m 1425m	1425m 1391s 1330s	1236m	1188w 1127s	990m	843m 757m	533m

Table-3:-Mass spectral data for Schiff base (SB-1)

m/e	%relative abundance
228	100 (Base peak)
227	10
212	15
197	15
189	18
185	18
181	18 (Parent peak)
155	35
154	75
144	25
136	65
122	45
110	62
98	60
97	15
95	100

Table-4:-Mass spectral data for Schiff base (SB-3)

m/e	%relative abundance
199	10 (parent peak)
189	05
164	10
155	28
154	100 (base peak)
150	40
138	30
137	52
136	70
107	22
95	15

Table -5:-Mass spectral data for Schiff base (SB-4)

m/e	%relative abundance
173	10
197	10
219	10
273	100 (base peak)
274	20
295	02
305	15
323	05
415	04
420	02
441	02

Table -6:-Mass spectral data for Schiff base (SB-5)

m/e	%relative abundance
173	100 (base peak)
174	20
189	04
195	10
205	03
211	04
227	04
278	03

Antimicrobial activities of the compounds under study:-

Procurement of pathogens:-ITCC certified Pathogens viz. Colletotrichumfalcatum (ITCC 6656) were procured from plant pathology division, I.A.R.I., New Delhi with due acknowledgement. Their sub- cultures have been made and the anti-microbial studies of the compounds under study were carried out against these pathogens at Birla Institute of Professional Studies with due acknowledgements. MIC (minimum inhibitory concentration) have been recorded which is then subjected to further studies to get QSAR equations. Experimental procedures that have been adopted for anti microbial studies are mentioned below:

Experimental procedure for Anti fungal studies:-

Pure culture of Colletotrichumfalcatum   obtained from I.A.R.I. was revived. Fresh inoculation of the fungal species was done by taking a loopful from I.A.R.I. culture tube and streaking was done on sterile PDA plates and slants and broth culture in sterile PDB incubated at ~24^{0}c for 5 -7 days to revive the culture. After revival of culture petri plates were prepared and for this purpose PDA was used. Media were cooled and plates were prepared by dispensing 15-20 mL media per plate. Plates were kept inverted in the incubator at ~24^{0}c overnight for sterility checking. Paper discs were made from whatmann filter paper using paper piercing instrument with a diameter of ~6mm and sterilized by keeping them in an incubator at ~70^{0}c for 24 hrs. About 100μL of actively growing pathogen from the culture was used to inoculate sterile PDA plates through spread plate method. The filter paper discs were dispensed on glass plates and each was loaded with 5 μL volume of pre decided dilution. These discs were left air dried in the laminar air flow and then carefully transferred to inoculated plates at pre designated positions. The plates were then inoculated at ~24^{0}c for 5-7 days.

Table-7:-Antifungal analysis of Schiff base compounds under study against Colletotrichumfalcatum
(ITCC NO-   6656)

Compounds under study	Concentrations Of compounds/10 ml			
	10 mg	**20 mg**	**30 mg**	**40 mg**
SB1	-------	---------	-------	-----
SB2	-------	---------	-------	-------
SB3	--------	----------	-------	10 mm
SB4	--------	----------	11mm	13 mm
SB5	--------	----------	--------	---------
SB6	---------	----------	--------	--------
SB7	---------	---------	---------	15mm
SB8	-------	---------	---------	10 mm
SB9	---------	----------	----------	-------
SB10	---------	20mm	29mm	30mm
SB11	---------	---------	----------	10 mm
SB12	-------	---------	--------	10 mm
SB13	--------	---------	18mm	20 mm
SB14	--------	---------	---------	-------
SB15	10mm	12mm	13mm	18 mm

Computational Details for the computational work:-

       The AM1Hamiltonia on Hyperchem 8.0 professional version were used to calculate the QSAR related descriptors such as Hydration energy (Hyd E), log P (log P), Refractivity (REF), Polarizability (POL). mass (mass), Surface area approx (SAA), Surface area Grid (SAG), volume (Vol), Heat of formation (HF) , Zero point energy (ZPE), HOMO energy (HOMO), LUMO energy (LUMO) and dipole moment (DM).

All these computations were carried out on Pentium core -2 duo machine having configuration
Intel (R) core $^{(TM)}$ 2 Duo CPU
T $_{5450}$@ 1.66 GHz.
982 MHz, 896 MB RAM
150 GB HDD
with windows – Microsoft windows XP software as an operating system.

       These descriptors and the activities of the compounds against specified microbes, mentioned in the tables, were taken into consideration in terms of p (MIC) and were subjected to statistical analysis/ regression analysis to get QSAR equations. All these statistical calculations were carried out on the same machine mentioned above using EXCEL software.

III.   Results and Discussion

       The in-vitro anti microbial viz. anti bacterial and anti fungal studies of the Schiff base compounds were carried out as per experimental procedure mentioned in the experimental section at Birla Institute of Professional Studies, Gwalior with due acknowledgement. The activities of the compounds were recorded in terms of Minimum Inhibitory Concentration (MIC). Some of the compounds have shown notable activities against the specified pathogen under study while other do not show any activity. The activities are recorded and reported here in the table 7. Figures of some of the plates were also taken showing growth of the pathogens..

       These labs.reported activities of the Schiff base compounds under study in terms of p(MIC) have been subjected to QSAR studies with Semi-empirical quantum chemical based certain parameters of the compounds. These parameters/ descriptors are hydration energy (HE), logP(logP), Refractivity(RF), Polarizaility (POL), Mass(Mass), Surface area approx(SAA), Surface area Grid(SAG), Volume (VOL), Heat of formation (HF), Zero point Energy (ZPE), HOMO energy(HOMO), LUMO energy   (LUMO) and dipole moment(DM).

       These parameters are computed on HYPERCHEM 8.0 version software after geometry optimization of the compounds under study as mentioned in the experimental section above. The computed parameters/ descriptors are reported in the tables 8-11.

       The methods adopted here in this project are AM1, PM3, MNDO and ZINDO respectively. All methods are proved to be good to give optimized geometry and minimized energy for the compounds under study. This fact can also be proved as IR studies which are observed experimentally for the compounds under study match well with the computed IR spectral frequencies using Hyperchem 8.0 professional software especially on the basis of AM1 and PM3 method. The fact of authenticity of AM1 and PM3 may prove to be appropriate in this study, so far as software is concerned.

       The software Hyperchem 8.0 version was quite fast and provides reasonably good results regarding all parameters viz. physical parameters, spectroscopic parameters and SAR related parameters.

Table-8 : Semi- Empirical AM1 based Computed properties of the Compounds (SB1-SB15) under study and their antifungal results p(MIC) on Colletotrichumfalcatum   (ITCC NO- 6656)

Compd	SAA	SAG	HE	Log P	RF	POL	Mass
SB-1	328.43	403.81	-5.27	1.7	63.44	22.15	182
SB-2	431.84	474.32	-4.13	0.75	77.06	27.17	225.29
SB-3	331.54	407.3	-10.03	0.67	65.05	22.79	198.22
SB-4	316.5	431.39	-5.44	-1.28	82.56	29.57	272.3
SB-5	307.6	373.6	-8.83	-0.13	53.02	19.31	172.19
SB-6	220.04	393.91	13.97	-0.31	58.09	21.34	188.23
SB-7	321.31	387.75	-5.91	0.13	64.08	22.15	182.22
SB-8	419.03	458.97	-4.74	-0.82	77.69	27.17	225.29
SB-9	511.03	396.31	25.91	-0.89	65.68	22.79	198.22
SB-10	410.85	489.58	-7.99	-2.85	83.2	29.57	272.3
SB-11	300.68	362.1	-9.65	-1.82	53.58	19.31	172.19
SB-12	320.5	387.2	-6.12	0.01	64	22.15	182.22
SB-13	418.19	459.23	-4.95	-0.94	-7.62	27.17	225.29
SB-14	191.46	382.67	-2.87	-1.02	65.61	22.79	198.22
SB-15	386.88	482.8	-8.37	-2.97	83.12	29.57	272.3

VOL	HF	ZPE	HOMO	LUMO	DM	MIC	P(MIC) obs.
625.06	90.6906	122.856	-0.6919	0.28678	0.846	40	-1.6021
756.97	93.4313	168.516	-0.4682	0.46352	2.391	40	-1.6021
637.89	41.6617	125.925	-0.6392	0.31279	1.173	40	-1.6021
708.65	93.8518	183.267	-0.0233	0.78834	10.492	30	-1.4771
565.99	64.5137	296.708	-0.5966	0.31456	0.518	40	-1.6021
624.46	83.3848	129.024	-1.0503	0.41409	1.739	40	-1.6021
603.63	93.2951	122.589	-0.8216	0.224	1.532	40	-1.6021
737.98	101.265	168.037	-0.5746	0.41979	3.794	40	-1.6021
636.32	72.8485	123.336	-0.9824	0.01622	0.04	40	-1.6021
850.52	24.9715	185.623	-0.0456	0.04697	3.247	20	-1.301
549.61	70.8844	103.81	-0.7422	0.21055	3.084	40	-1.6021
604.65	93.9724	122.609	-0.8569	0.15012	3.463	40	-1.6021
736.8	101.813	168.075	-0.6006	0.36356	6.029	30	-1.4771
606.8	115.656	123.955	-0.1917	0.22419	3.773	40	-1.6021
813.78	25.1947	185.703	-0.5742	0.07244	2.504	10	-1

Table -9: Semi- Empirical PM3 based Computed properties of the Compounds (SB1-SB15) under study and their antifungal results p(MIC) on Colletotrichumfalcatum (ITCC NO- 6656)

Compd	MIC	P(MIC)Obs.	SAA	SAG	HE	Log P	RF
SB-1	10	-1.6021	327.9	398.57	-5.21	1.7	63.44
SB-2	40	-1.6021	429.81	471.29	-4.09	0.75	77.06
SB-3	40	-1.6021	330.69	405.7	-10.08	0.67	65.05
SB-4	40	-1.4771	421.13	487.55	-6.75	-1.28	82.56
SB-5	40	-1.6021	308.07	373.46	-8.7	-0.13	53.02
SB-6	10	-1.6021	240.24	396.48	15.86	-0.31	58.09
SB-7	10	-1.6021	321.22	386.16	-5.91	0.13	64.08
SB-8	40	-1.6021	407.33	448.7	-4.5	-0.82	77.69
SB-9	40	-1.6021	806.97	394.77	31.12	-0.89	65.58
SB-10	40	-1.301	346.15	448.96	-6.48	-2.85	83.2
SB-11	40	-1.6021	300.33	358.64	-9.57	-1.82	53.58
SB-12	30	-1.6021	320.33	386.98	-6.11	0.01	64
SB-13	30	-1.4771	300.14	463.82	-3.11	-0.94	77.62
SB-14	40	-1.6021	-637.25	399.25	21.37	-1.02	65.61
SB-15	40	-1	438.28	494.15	-8.31	-2.97	83.12

POL	Mass	VOL	HF	ZPE	HOMO	LUMO	DM
22.15	182.22	617.65	74.5392	118.0805	-0.0237	0.26053	0.856
27.17	225.29	751.72	75.0653	161.0597	-0.6047	0.12665	1.636
22.79	198.22	635.43	31.13328	121.3319	-0.7363	0.07505	0.576
2.57	272.3	808.85	23.0389	177.9144	-0.1781	0.2533	3.178
19.31	172.19	565.62	45.417	298.6673	-0.6761	0.01641	0.0695
21.34	188.23	626.51	67.5881	123.476	-1.1512	0.26996	1.601
22.15	152.22	601.46	84.0827	117.0909	-0.908	0.000038	1.271
27.17	225.29	733.56	73.9653	163.41169	-0.4841	0.05898	2.219
22.79	198.22	637.16	69.1811	118.1698	-0.0854	0.18165	0.219
29.57	272.3	761.35	20.0201	180.9994	-0.2461	0.06722	3.985
19.31	172.19	547.72	53.6628	99.6895	-0.8176	0.05231	3.093
22.15	182.22	601.83	84.5714	17.8388	-0.9709	0.005465	3.068
27.17	237.3	764.27	19.88857	166.303	-0.2295	0.19077	4.018
22.79	198.22	639.93	82.8752	118.0187	-0.1425	0.1323	2.432
29.57	272.3	818.5	17.18738	177.1228	-0.0148	0.10017	3.332

Table-10: Semi- Empirical MNDO based Computed properties of the Compounds (SB1-SB15) under study and their antifungal results p(MIC) on Colletotrichumfalcatum (ITCC NO- 6656)

Compd	MIC	P(MIC)Obs.	SAA	SAG	HE	Log P	RF
SB-1	40	-1.6021	330.44	398.47	-5.25	1.7	63.44
SB-2	40	-1.6021	431.87	474.32	-4.13	0.75	77.06
SB-3	40	-1.6021	334.34	409.26	-10.21	0.67	65.05
SB-4	30	-1.4771	390.26	501.86	-7.57	-1.28	82.56
SB-5	40	-1.6021	308.07	372.46	-8.7	-0.13	53.02
SB-6	40	-1.6021	363.32	421.19	28.06	-0.31	58.09
SB-7	40	-1.6021	325.42	390.74	-6	0.13	64.05
SB-8	40	-1.6021	424.74	461.48	-4.85	-0.82	77.69
SB-9	40	-1.6021	335.53	410.08	11.66	-0.84	65.69
SB-10	20	-1.301	441.86	516.88	-8.45	-2.85	83.2
SB-11	40	-1.6021	516.88	364.47	-9.63	-1.82	53.58
SB-12	40	-1.6021	324.51	390.82	-6.13	0.01	64

SB-13	30	-1.4771	424.08	462.98	-5.04	-0.94	77.62
SB-14	40	-1.6021	85.62	385.41	-2.18	-1.02	65.61
SB-15	10	-1	373.02	493.92	-8.61	-2.97	83.12

POL	Mass	VOL	HF	ZPE	HOMO	LUMO	DM
22.15	182.22	620.52	72.6814	125.5213	-0.7304	0.1807	0.115
27.17	225.29	756.97	83.6483	173.1405	-0.552	0.3057	1.985
22.79	198.22	639.44	26.4478	128.8318	-0.6656	0.164	1.313
29.57	272.3	831.31	86.8148	187.9244	-0.2584	0.7191	9.788
19.31	172.19	565.62	37.5895	294.6581	-0.5852	0.2013	0.256
21.34	188.23	653.43	77.1433	132.8215	-1.0426	0.2484	1.872
22.15	182.22	607.45	90.8727	125.2745	-0.8436	0.0489	1.666
27.17	225.29	744.34	1-1.5124	172.8898	-0.6482	0.2094	3.487
22.79	198.22	653.5	76.8839	126.1077	-0.111	0.0129	0.94
29.57	271.3	851.71	39.9456	190.328	-0.1264	0.0924	2.72
19.31	172.19	552.73	54.2342	106.3981	-0.7498	0.1216	3.434
22.15	182.22	608.03	99.2275	125.2744	-0.0444	0.07092	3.738
27.17	225.29	745.39	101.729	172.9119	-0.7083	0.12267	5.8
22.79	198.22	611.87	118.4008	127.213	-0.3373	0.06016	3.922
29.57	272.3	829.41	67.5956	189.1327	-0.911	0.7773	9.452

Table -11: Semi- Empirical ZINDO based Computed properties of the Compounds (SB1-SB15) under study and their antifungal results P(MIC) on Colletotrichumfalcatum (ITCC NO- 6656)

Compd	MIC	P(MIC)Obs.	SAA	SAG	HE	Log P	RF
SB-1	40	-1.6021	326.31	398.74	-5.13	1.7	63.44
SB-2	40	-1.6021	424.59	468.15	-3.98	0.75	77.06
SB-3	40	-1.6021	328.99	410.75	-9.8	0.67	65.05
SB-4	30	-1.4771	302.76	441.39	-7.29	-1.29	82.56
SB-5	40	-1.6021	304.93	369.03	-8.63	-0.013	53.02
SB-6	40	-1.6021	-181.81	374.77	-8.95	-0.31	58.09
SB-7	40	-1.6021	319.51	385.78	-5.81	0.13	64.08
SB-8	40	-1.6021	417.14	454.99	-4.72	-0.82	77.69
SB-9	40	-1.6021	208.81	396.28	-7.19	-0.89	65.68
SB-10	20	-1.301	369.07	456.56	-7.15	-2.85	83.2
SB-11	40	-1.6021	296.07	355.04	-9.52	-1.82	53.08
SB-12	40	-1.6021	318.2	381.79	-6.09	0.01	64
SB-13	30	-1.4771	415.76	455.86	-4.93	-0.94	77.62
SB-14	40	-1.6021	-515.87	371.28	557.06	-1.02	65.61
SB-15	10	-1	320.41	440.74	-7.49	-2.49	83.12

POL	Mass	VOL	HF	ZPE	HOMO	LUMO	DM
22.15	183.22	614.22	-5357.263	166.065	-7.266	5.3892	0.767
27.17	225.29	744.51	-6733.5149	229.561	-5.7525	5.6997	1.445
22.29	198.22	636.3	-5499.3121	169.919	-7.177	5.8793	2.46
29.57	272.3	735.94	-7446.8667	255.6673	-4.8535	5.0977	3.882
19.31	172.19	561.53	-4598.1684	328.6815	-6.9848	5.6676	1.415
21.34	188.23	584.88	-5392.7584	180.5573	-5.7055	4.316	1.846
22.15	182.22	599.51	-5342.8922	166.099	-6.8912	5.4596	1.358
27.17	225.29	729.78	-6719.1172	229.5434	-5.7808	5.7748	3.079
22.79	198.22	620.61	-5502.9938	170.1358	-6.8308	5.0378	7.069
29.57	272.3	770.33	-7388.4733	252.558	-6.6451	5.8622	2.089
19.31	172.19	542.8	-4583.9114	140.7262	-7.2156	5.4445	3.347
22.15	182.22	599.36	-5344.7538	166.1238	-7.2369	5.1767	3.849
27.17	225.29	728.99	-6721.2763	229.5709	-5.9184	5.4844	5.915
22.79	198.22	590.34	-5460.0367	169.2597	-3.8549	6.7071	4.554
29.17	272.3	741.15	-7519.3218	253.8556	-4.1665	6.5701	7.667

This final equation was used to get predicted activities for all the series of compounds and against all microorganisms under study. The final 3D QSAR equations are reported as under:-

AM1/Schiff base compounds (SB1-SB15)/Antifungal Colletotrichumfalcatum (ITCC NO- 6656) **/3D-equation**

P(MIC) = -0.058595368(LogP)+0.000791347(Mass)+0.000632045(VOL)-2.154266796
N = 15, SD = 0.104560234, r = 0.834310522, F test = 8.397675409

PM3/Schiff base compounds (SB1-SB15)/Antifungal Colletotrichumfalcatum (ITCC NO- 6656) **/3D-equation**

P(MIC) = -0.05113144(LogP)+0.001480447(Mass)-0.001375507(HF)-1.793867934
N = 15, SD = 0.107689734, r = 0.823169914, F test = 7.706676044

MNDO/Schiff base compounds (SB1-SB15)/Antifungal Colletotrichumfalcatum   (ITCC NO- 6656) **/3D-equation**
P(MIC) = -0.037797391(LogP)+0.003834886(Mass)-0.000507095(VOL)-2.01860159
N = 15, SD = 0.107080072, r = 0.825377898, F test = 7.836553464

ZINDO/Schiff base compounds (SB1-SB15)/Antifungal Colletotrichumfalcatum   (ITCC NO- 6656) **/3D-equation**
P(MIC) = -0.037797391(LogP)+0.0041666(Mass)+5.2409E-05(HF)-2.11514388
N = 15, SD = 0.112498247, r = 0.805093409, F test = 6.755193075

Graphs were also drawn between observed activities and predicted activities, both in the terms of p(MIC) form 3 D-QSAR equations for this series of compounds. These trend line graphs are shown in figure 3-6.

IV.   Conclusions

This method has once again proved to be useful for this type of studies. The parameters/ descriptors which contribute positively to p (MIC) in final 3D QSAR equations are listed below:-
AM1/ Schiff bases (SB1-SB15)/ Colletotrichumfalcatum   (ITCC NO- 6656)**: -** Log P , Mass and VOL
PM3/ Schiff bases (SB1-SB15)/ Colletotrichumfalcatum   (ITCC NO- 6656)**: -** Log P , Mass and HF
MNDO/ Schiff bases (SB1-SB15)/ Colletotrichumfalcatum   (ITCC NO- 6656)**:** Log P , HE and VOL
ZINDO/ Schiff bases (SB1-SB15)/ Colletotrichumfalcatum   (ITCC NO- 6656)**:** Log P , DM and HF

In conclusion this may be said that these parameters / descriptors have more impact on (MIC) over all other descriptors computed and reported.

Acknowledgements

Figure -3 Trend line Graph between p(MIC) observed and AM1 computed p(MIC) calculated for the Schiff base compounds (SB1-SB15)under study for their antifungal activities on Colletotrichumfalcatum (ITCC NO- 6656)
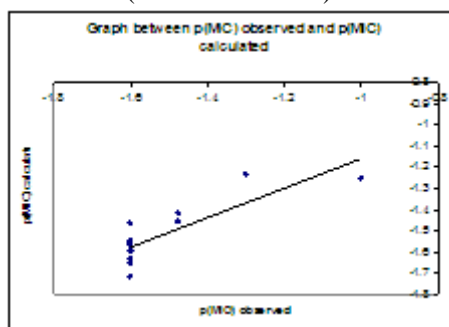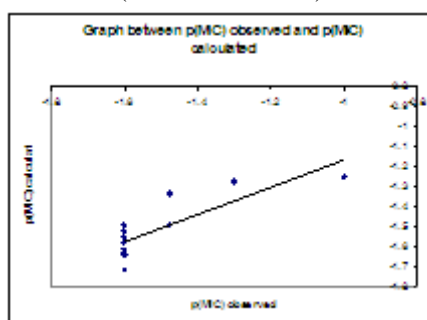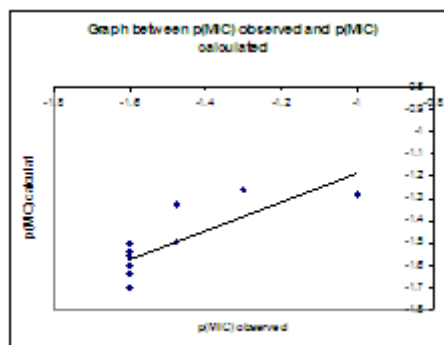

p(MIC) obsered	p(MIC) calculated
-1.602	-1.715
-1.602	-1.541
-1.602	-1.633
-1.477	-1.416
-1.602	-1.653
-1.602	-1.592
-1.602	-1.636
-1.602	-1.461
-1.602	-1.543
-1.301	-1.234
-1.602	-1.564
-1.602	-1.628
-1.477	-1.455
-1.602	-1.554
-1	-1.25

Figure -4 Trend line Graph between p(MIC) observed and PM3 computed p(MIC) calculated for the Schiff base compounds (SB1-SB15)under study for their antifungal activities on Colletotrichumfalcatum (ITCC NO-   6656)
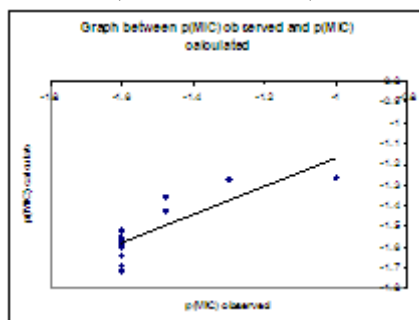
P(MIC) (Observed)	P(MIC) (Calculated)
-1.602	-1.714
-1.602	-1.602
-1.602	-1.577
-1.477	-1.357
-1.602	-1.595
-1.602	-1.592
-1.602	-1.691
-1.602	-1.52
-1.602	-1.55
-1.301	-1.273
-1.602	-1.52
-1.602	-1.641
-1.477	-1.422
-1.602	-1.562
-1	-1.263

Figure-5 Trend line Graph between p(MIC) observed and MNDO computed p(MIC) calculated for the Schiff base compounds (SB1-SB15)under study for their antifungal activities on Colletotrichumfalcatum (ITCC NO-   6656)

p(MIC) observed	p(MIC) calculated
-1.602	-1.717
-1.602	-1.575
-1.602	-1.615
-1.477	-1.334
-1.602	-1.639
-1.602	-1.613
-1.602	-1.634
-1.602	-1.492
-1.602	-1.549
-1.301	-1.272
-1.602	-1.551
-1.602	-1.629
-1.477	-1.487
-1.602	-1.519
-1	-1.251

Figure -6 Trend line Graph between p(MIC) observed and ZINDO computed p(MIC) calculated for the Schiff base compounds (SB1-SB15)under study for their antifungal activities on Colletotrichumfalcatum
(ITCC NO-   6656)

p(MIC) observed	p(MIC) calculated
-1.602	-1.697
-1.602	-1.558
-1.602	-1.603
-1.477	-1.322
-1.602	-1.638
-1.602	-1.602
-1.602	-1.641
-1.602	-1.498
-1.602	-1.544
-1.301	-1.26
-1.602	-1.569
-1.602	-1.636
-1.477	-1.493
-1.602	-1.537
-1	-1.281

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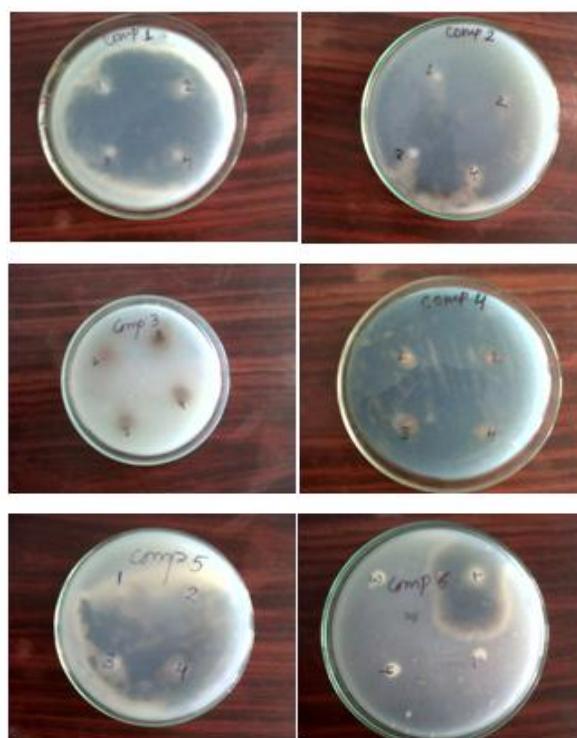[33]. KishorArora, Int J Pharm Bio Sc.,5 (3) : 138 – 148, (2014).

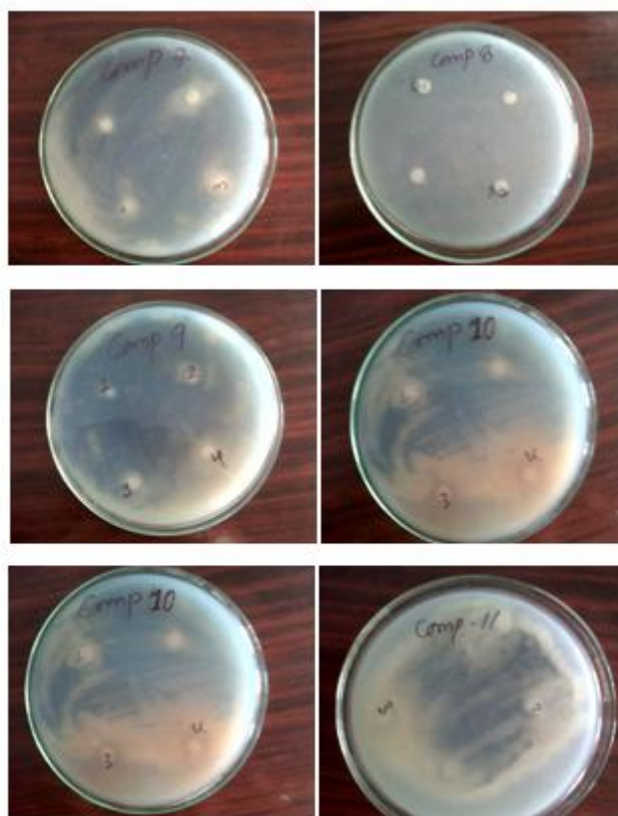**Figure -1:** Some notable photographs for anti fungal studies of compounds under study

Figure -2: Some notable photographs for anti fungal studies of compounds under study