Int J Pharm Bio Sci 2015 Jan; 6(1): (P) 188 - 203

Research Article **Chemistry**

International Journal of Pharma and Bio Sciences

ISSN 0975-6299

ANTI-FUNGAL AND 3D-QSAR STUDIES FOR SOME PYRAZOLONES

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ABSTRACT

3 Descriptor quantitative structure and activity relationship (3d-QSAR) studies for a series of pyrazolone compounds using their semi-empirical quantum chemically derived descriptors and their laboratory reported activities against pathogen viz. *Colletotrichum falcatum* (ITCC 6656) have been carried out and reported in this present paper. Graphs between observed and predicted activities, both in the terms of p(MIC)*cal* and p(MIC) *obs.* viz.-log (MIC) are reported. This is concluded on the basis of these graphs that some of the descriptors computed and taken into account in the present paper have positive contribution towards the activities. The method has been proved to be useful tool for such type of studies.

KEYWORDS: Semi-empirical/3D-qsar/fungal pathogen/pyrazolones

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INTRODUCTION

Medicinal chemists are 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), 3D-QSAR, 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.QSAR viz.. Quantitative structure and activity relation ship has been developed and reported as a technique based on statistical analysis of some physical/ other descriptors to predict the models for designing new drugs/ compounds active against pathogens. In some of the recent references workers have reported QSAR studies with quantum chemically viz. ab-initio and semiempirical reported descriptors and correlated these descriptors with lab reported activities of the compounds against a certain micro-organism, which has been proved as a step ahead in the related field. Pyrazoles refer to the class of compounds which are heterocyclic compounds characterized by 5-membered ring structure composed of three carbon and two nitrogen atoms in the adjacent position to the two nitrogen atoms, one is basic and second is neutral nitrogen, the aromatic nature arises from the four electrons and the unshared pair of electrons on the NH nitrogen. Pyrazolone compounds and their derivatives have been reported by a number of workers as compounds with antiinflammatroy and other reported medicinal activities. Due to wide range of biological activity, pyrazoles have received a considerable interest in the field of drug discovery and therefore, pyrazole ring constitutes a relevant synthetic target in pharmaceutical industry. In fact such a heterocyclic moiety represents the core structure of a number of drugs. The Literature survey carried out in the proposed field (1-32) revealed that on one side the workers/ scientists have tried many naturally occurring and synthetic compounds to check their activities against various microorganisms while on the other 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 even 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. pyrazolone compounds shown in figure 1 with their activities against Colletotrichum falcatum (ITCC 6656) are reported.

Experimental

Preparation of pyrazolone compounds

Some of the Pyrazolone compounds were prepared in the laboratory while some were obtained from standard sources as E Merck, C.D.H. and B.D.H. etc. and were used as such for further work.

Processes of synthesis of synthesized pyrazolones are given below:

3- Methyl -5- pyrazolone (MeP)

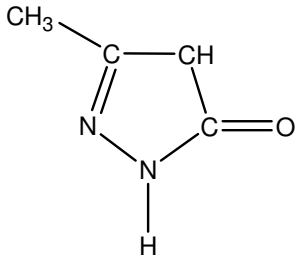
Hydrazine hydrate (50%solution, approx. 4 ml) was taken in a beaker with diethyl ether (20 ml) and ethyl acetoacetate (8 ml) was added to it drop wise in order to avoid the vigorous reaction. White crystalline solid separated out within one minute. It was then filtered and washed with diethyl ether, 3 to 4 times. On exposing to air surface oxidation of the compound may take place and compound becomes pink (yield ~95%).

3- Methyl-4-Nitroso-5- pyrazolone (MNP)

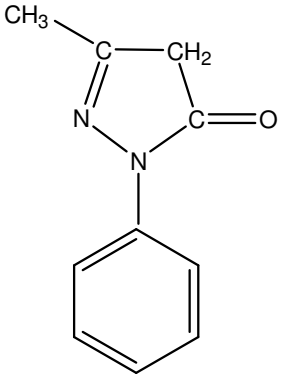
Above procured pyrazolone (2g) was dissolved in a minimum amount of (1:1) acetic acid in a conical flask. This was then kept in an ice bath for about 15 minutes, so that the temperature of the solution was brought down to 10^0C. Solid sodium nitrite (4g) was added in portions to this solution. Precipitate was obtained immediately but the reaction mixture was kept in the ice bath with stirring for 1 hour. The product was then filtered and washed with dilute acetic acid followed by water and was re- crystallized from (1:1) aq. Methyl alcohol and yellow product was obtained (yield ~70%).

3- Methyl- 1-(2,4-di nitrophenyl)-5-pyrazolone

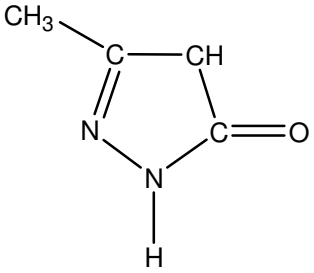
A mixture of phenyl hydrazine/ 2,4-dinitrophenyl hydrazine (0.01 mol) and thylacetoacetate (0.01 mol) were taken in absolute alcohol (30 mL) and refluxed for 12 hrs. After completion of the reaction, excess of solvent was distilled off and the resultant residue was poured on crushed ice to obtain the yellow/ orange long needle shaped crystals. Solids precipitated were filtered and re-crystallized using ethanol (yield~70%) (70-71). Compounds pyrazolones (Py1-Py7) which are under study in this present paper are shown in the figure. Analytical studies were also carried out for the synthesized pyrazolone compounds under study. These are given in the tables 1 along with their melting points.



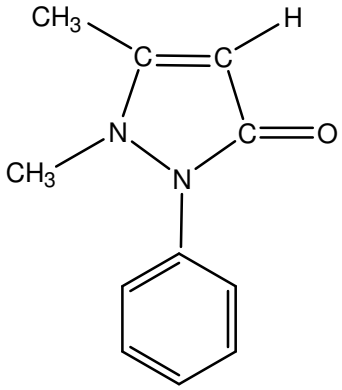
3-methyl-5-pyrazolone (PY1)



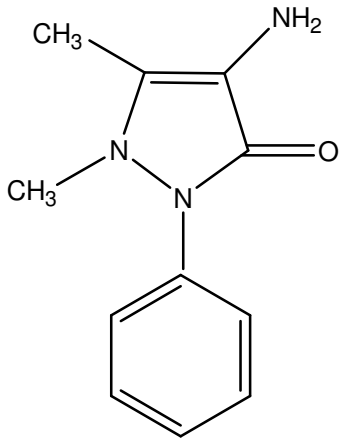
3-Methyl-l-phenyl-5-Pyrazolone (PY2)



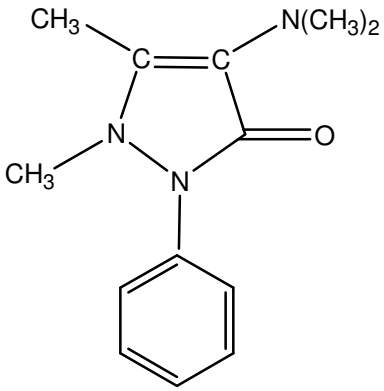
3-Methyl-4-nitroso-5-pyradolone (Py3)



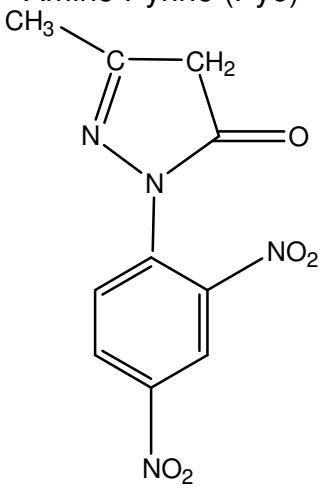
Antiprine (Py4)



4-Aminoantipyrine (PY5)



Amino Pyrine (Py6)



3-Methyl – 1 (2,4-dinitrophenyl)5-pyrazolone (Py7)

Figure 1
Pyrazolone Compounds under study

Table 1
Analytical studies for the Pyrazolone compounds under study

Compound	M. Pt. (^{0}C)	C Found (Calcd.)	H Found (Calcd.)	N Found (Calcd.)
Py-1	224-226	49.85 (49%)	6.04 (5.1%)	28.20 (28.8%)
PY-2	124-126	71.59 (69%)	5.65 (5.7%)	16.32 (16.0%)
PY-3	229-231	39.88 (42.0%)	2.899 (4.0%)	32.97 (33.0%)
PY-4	110-115	71.50 (70.2%)	6.43 (6.3%)	14.73 (14.8%)
PY-5	105-110	66.97 (65.0%)	6.32 (6.4%)	19.64 (20.69%)
PY-6	107-108	67.59 (67.5%)	7.24 (7.3%)	17.52 (18.1%)
PY-7	81-88	57.49 (48.0%)	6.35 (4.9%)	20.04 (20.0%)

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 -4 for pyrazolone compounds. I.R. spectral analysis shows that (C=O) Stretching is the predominant peak in the case of pyrazolone compounds under study. It appears at about 1660-1610 cm^{-1}. Apart from these peaks some other notable peaks are ring stretching of 5 membered ring, Ring stretching, CH out of plane deformation of pyrazolone ring, C=O in plane bending and out of plane bending etc. These are reported in the table 2.

Table 2
IR spectral analysis for the Pyrazolones under study

Assignment/ Compound	(C=O) Stretching	Ring stretching Of 5 membered ring	Ring stret-ching	CH out of plane defor-mation of pyrazolone ring	Out of plane ring deform-ation	C=O in plane bending	Out of plane bending of ring	C=O out of pane bending
Py-1	1623s	1553s 1500s 1444.9s	1255w 1195w 1165.9m	1090sh 1011m	974w 833w 753s	753s	612.2m	523.7w 504w
PY-2	1610.7s	1522w 1457w 1394w	1394w 1198w	1076m 1025w	917s 800w 757w	689w	616m	570s 499.5m
PY-3	1615s	1562w 1515w 1466m	1371m 1290w 1168w	1089m 1034s	980w 872w 765s	657.9w	601w	564w 499w
PY-4	1630m	1585m 1444w	1360m 1275m 1188w	1125m	920w 753m	616m	603w	570m
PY-5	1649m	1594m 1444w 1350m	1350m 1275m 1178w	1115m	920w 753m	661m	------	572m
PY-6	1657s	1474m 1317w	1317w 1198w	1111m	954w 750w	695m	604m	559m 500m
PY-7	1614s	1562m 1519m 1442w	1367w 1253w 1192m	1117m	973w 779m 754w	709m	612w	527m 452w

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:-

Py1: 1.150-1.105 (t); 2.430-2.011 (q); 3.997-3.974 (d);5.140-(s);6.005 (s); 10.277(s).
Py2:- 2.110 (s); 2.500 (s); 3.329 (s); 3.327-3.696 (d); 5.349 (s); 7.817-7.174 (multiplet).
Py5:-2.083 (S); 2.723-2.489(d); 3.333(s); 3.842 (s); 7.4445-7.219 (q).

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 , Py-1:- 79, Py-2 :-175, Py-3:- 127 and Py-5:-203 with parent ion peaks at Py-1:- 98, Py-2 :-174, Py-3:- 127 and Py-5:-203.. These parent peaks confirm the mol. weights of the compounds under study

Antimicrobial activities of the compounds under study

Procurement of pathogens

TCC certified Pathogens viz. *Colletotrichum falcatum* (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 *Colletotrichum falcatum* 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 ~24^0c for 5 -7 days to revive the culture. After the 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 ~24^0c 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 ~70^0c 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 volumes 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 ~24^0c for 5-7 days.

Table 3
Antifungal analysis of pyrazolone compounds under study against Colletotrichum falcatum (ITCC NO- 6656)

Compounds under study	Concentrations Of compounds/10 ml			
	10 mg	20 mg	30 mg	40 mg
PY1	10mm	13 mm	19mm	20mm
PY2	11mm	13mm	18mm	20 mm
PY3	11mm	12mm	14mm	15 mm
PY4	--------	----------	-------	--------
PY5	11mm	13 mm	19 mm	21 mm
PY6	--------	---------	---------	-------
PY7	--------	12mm	15 mm	19 mm

Computational Details for the computational work

The AM1 Hamiltonia 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.

RESULTS AND DISCUSSION

The *in-vitro* anti fungal studies of the pyrazolone 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 does not show any activity. The activities are recorded and reported here in the table 3. Figures of some of the plates were also taken showing growth of the pathogens.These lab reported activities of the pyrazolone 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 4-7. 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 4

Semi- Empirical AM1 based Computed properties of the Compounds (Py1-Py7) under study and their antifungal results p(MIC) on Colletotrichum falcatum (ITCC NO- 6656)

Compd	MIC	P(MIC)Obs.	SAA	SAG	HE	Log P	RF
Py-1	10	-1	231.64	256.11	-5.19	0.2	24.82
Py-2	10	-1	310.59	365.51	-2.13	0.94	54.3
Py-3	10	-1	258.75	274.11	-11.31	0.17	29.75
Py-4	40	-1.6021	339.82	385.49	-1.84	-0.4	61.23
Py-5	10	-1	336.88	399.17	-6.51	-1.99	64.85
Py-6	40	-1.6021	448.38	474.55	-1.58	-1.22	74.92
Py-7	20	-1.301	393.51	449.94	-10.14	-2.03	73.66

POL	Mass	VOL	HF	ZPE	HOMO	LUMO	DM
9.71	98.1	351.97	4.99398	64.831	-9.5347	0.19945	2.617
19.37	174.2	565.04	44.6349	117.65	-8.6403	0.09622	2.781
10.92	127.1	391.94	19.26134	641.09	-0.1633	0.8305	2.298
21.4	188.23	608.04	63.6532	135.458	-0.1844	0.48155	4.438
22.78	203.24	640.43	60.5788	161.421	-0.0912	0.4694	3.423
26.45	231.3	770.61	73.3708	179.1184	-0.04307	0.44813	10.224

Table 5

Semi- Empirical PM3 based Computed properties of the Compounds (Py1-Py7) under study and their antifungal results p(MIC) on Colletotrichum falcatum (ITCC NO- 6656)

Compd	MIC	P(MIC)Obs.	SAA	SAG	HE	Log P	RF
Py-1	10	-1	231.61	253.25	-5.27	0.2	24.82
Py-2	10	-1	311.61	367.05	-2.12	0.94	54.3
Py-3	10	-1	260.44	275.75	-11.48	0.17	29.75
Py-4	40	-1.6021	341.81	393.51	-1.85	-0.4	61.23
Py-5	10	-1	338.91	403.98	-6.64	-1.99	64.85
Py-6	40	-1.6021	450.08	479.24	-1.53	-1.22	74.92
Py-7	20	-1.301	392.41	453.99	-10.28	-2.03	73.66

POL	Mass	VOL	HF	ZPE	HOMO	LUMO	DM
9.71	98.1	349.99	10.0348	61.83218	-0.0272	1.0386	2.46
19.37	174.2	565.41	20.69754	112.6618	-0.1096	0.1388	2.607
10.92	127.1	392.83	11.62258	61.7474	-0.3937	0.3769	2.112
21.43	188.23	613.4	22.7265	130.4475	-0.2538	0.2318	4.053
22..78	203.24	644.42	21.3358	141.3387	-0.2158	0.2368	3.336
26.45	231.3	770.89	51.0475	173.459	-0.0148	1.1074	10857
24.36	278.22	737.64	1.2.26173	133.1422	-0.2813	0.04362	10.665

Table 6

Semi- Empirical MNDO based Computed properties of the Compounds (Py1-Py7) under study and their antifungal results p(MIC) on Colletotrichum falcatum (ITCC NO- 6656)

Compd	MIC	P(MIC)Obs.	SAA	SAG	HE	Log P	RF
Py-1	10	-1	231.86	255.82	-5.15	0.2	24.82
Py-2	10	-1	312.51	367.73	-2.01	0.94	54.3
Py-3	10	-1	260.81	278.31	-11.36	0.17	29.75
Py-4	40	-1.6021	340.57	398.37	-1.84	-0.4	61.23
Py-5	10	-1	339.38	414.33	-6.4	-1.99	64.85
Py-6	40	-1.6021	454.12	483.23	-1.58	-1.22	74.92
Py-7	20	-1.301	386.92	458.83	-9.7	-2.03	73.66

POL	Mass	VOL	HF	ZPE	HOMO	LUMO	DM
9.71	98.1	352.87	18.9028	67.243	-9.7772	0.0215	2.153
19.37	174.2	569.02	16.0375	121.0237	-0.0345	0.14629	2.261
10.92	127.1	395.23	7.4868	66.9777	-0.3169	0.6199	1.963
21.43	188.23	621.48	28.7572	139.841	-0.2134	0.1405	3.706
22.78	203.24	658.47	28.6354	151.104	-0.2951	0.0574	2.868
26.45	231.3	784.55	70.6098	184.9554	-0.4308	0.36126	10.653
24.86	278.22	753.34	118.9328	143.7598	-0.07829	0.01692	9.536

Table 7

Semi- Empirical ZINDO based Computed properties of the Compounds (Py1-Py7) under study and their antifungal results p(MIC) on Colletotrichum falcatum (ITCC NO- 6656)

Compd	MIC	P(MIC)Obs.	SAA	SAG	HE	Log P	RF
Py-1	10	-1	231.39	252.79	-5.33	0.2	24.82
Py-2	10	-1	306.03	360.91	-2.13	0.94	54.3
Py-3	10	-1	229.25	264.75	-7.42	0.17	29.75
Py-4	40	-1.6021	333.51	377.65	-1.85	-0.4	61.23
Py-5	10	-1	332.91	392.87	-6.54	-1.99	64.85
Py-6	40	-1.6021	368.17	438.18	-4.37	-1.22	74.92
Py-7	20	-1.301	393.59	427.05	-10.08	-2.03	73.66

POL	Mass	VOL	HF	ZPE	HOMO	LUMO	DM
9.71	98.1	349.67	-2425.099	89.403	-6.7886	6.9301	3.918
19.37	174.2	557.74	-4915.264	160.01	-6.063	6.84	4.398
10.92	127.1	372.98	-2738.509	89.95	-6.8543	6.1565	6.832
21.43	188.23	592.26	-5450.551	184.983	-5.8917	6.6588	7.057
22.78	717.28	626.64	-5727.0466	199.149	-5.5803	6.6033	5.953
26.45	231.3	717.28	-6723.9806	248.19	-5.3664	7.3694	7.905
24.86	278.22	689.05	-6433.8554	193.0471	-3.2596	4.1054	19.919

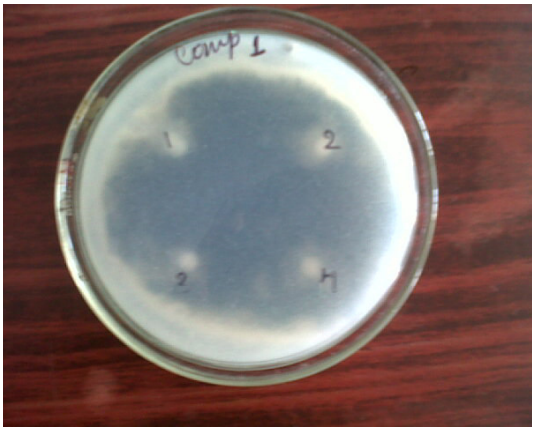
This final equation was used to get predicted activities for all the series of compounds and against the microorganism under study. The final 3D QSAR equations are reported as under:

AM1/Pyrazolones compounds (Py1-Py7)/Antifungal
Colletotrichum falcatum (ITCC NO- 6656) /3D-equation
P(MIC) = -0.008303662(SAA)+0.004792134(SAG)+0.007116235(DM)-0.283944849
N = 7, SD = 0.248775203, r = 0.78903441, F test = 1.649535123

PM3/Pyrazolones compounds (Py1-Py7)/Antifungal
Colletotrichum falcatum (ITCC NO- 6656) /3D-equation
P(MIC) = -0.053854562(SAG)+0.027237075(VOL)-2.26487E-05(SAA)+3.147351075
N = 7, SD = 0.21199324, r = 0.852015753, F test = 2.64871411

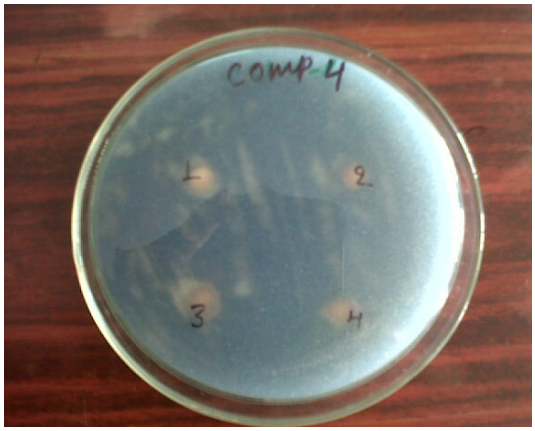
MNDO/Pyrazolones compounds (Py1-Py7)/Antifungal
Colletotrichum falcatum (ITCC NO- 6656) /3D-equation
P(MIC) = -0.010818651(SAA)-0.0703233(HF)-0.012483293(ZPE)+796941162
N = 7, SD = 0.27108534, r = 0.742862735, F test = 1.231371059

ZINDO/Pyrazolones compounds (Py1-Py7)/Antifungal
Colletotrichum falcatum (ITCC NO- 6656) /3D-equation
P(MIC) = -0.010818651(SAA)-0.000703233(HF)-0.012483293(ZPE)+0.79694112
N = 7, SD = 0.260493319, r = 0.765625272, F test = 1.416251604
Graphs were also drawn between observed activities and predicted activities, both in the terms of p(MIC) viz.-log (MIC) form 3 D-QSAR equations for this series of compounds. These trend line graphs are shown in figure 3-6.


Comp 1
1
2
3
4


Comp 2
1
2
3
4


Comp 3
1
2
3
4


Comp 4
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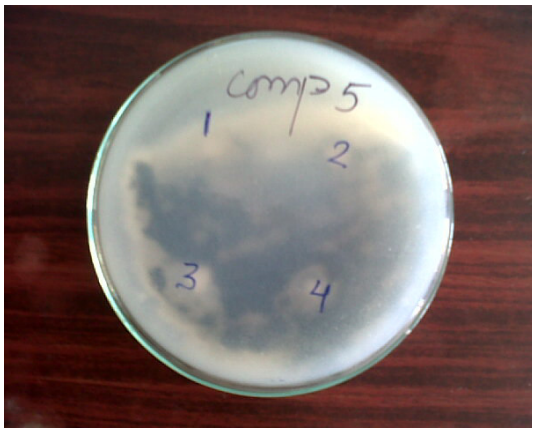
Comp 5
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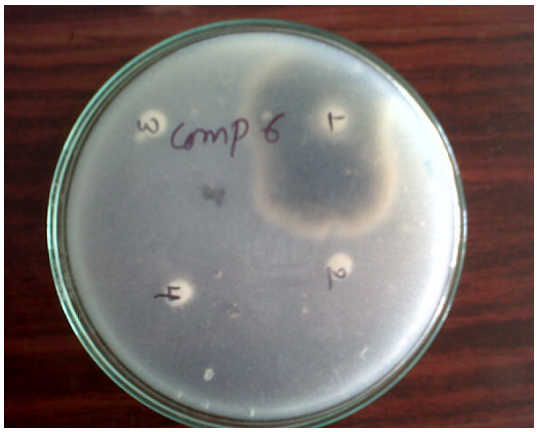

Comp 6

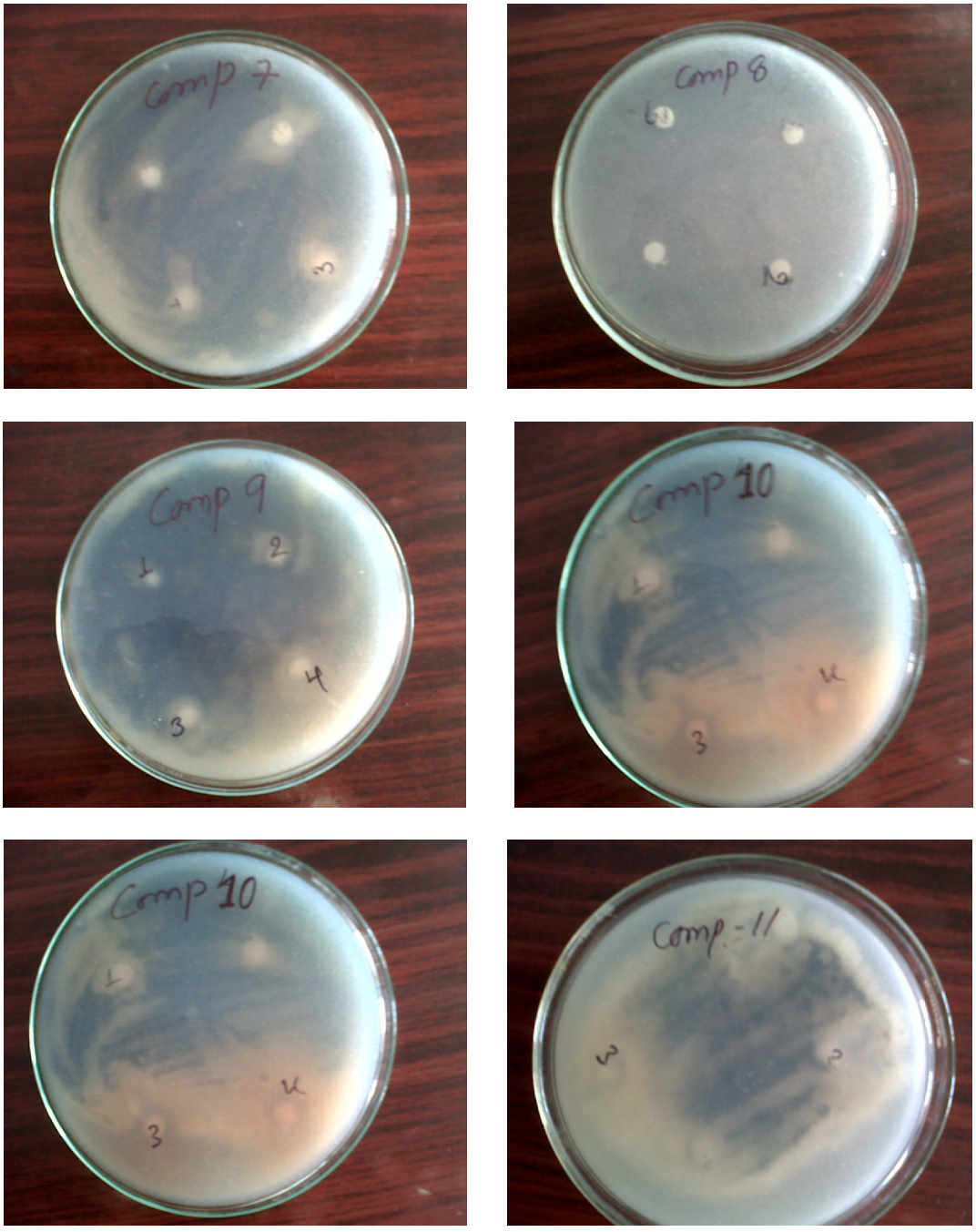
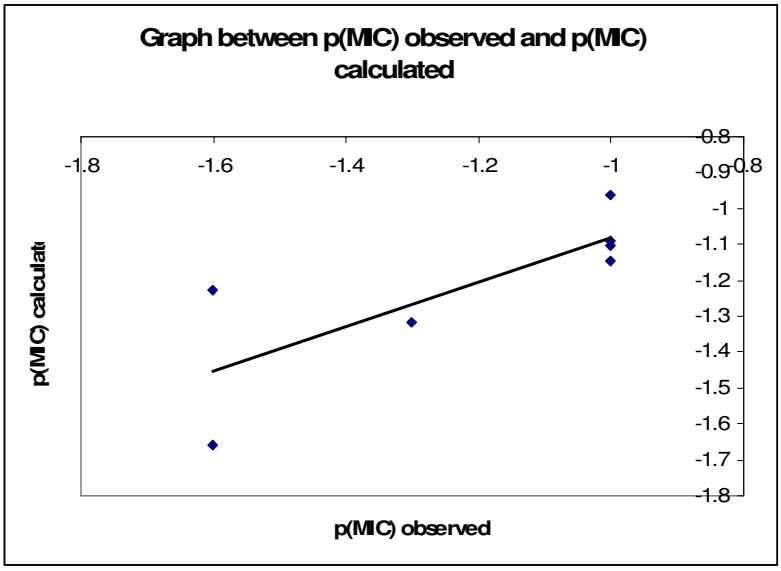


Figure 2
Some notable photographs for anti fungal studies of compounds under study

Figure 3

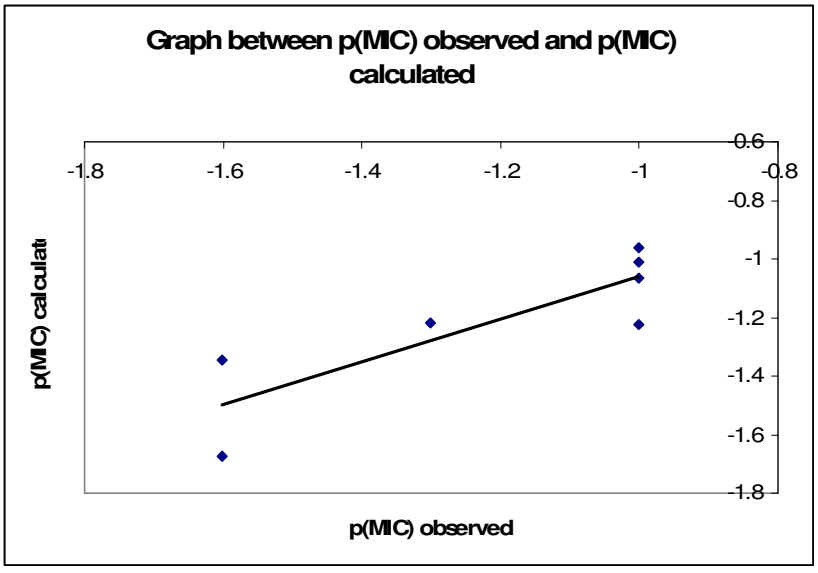
Trend line Graph between p(MIC) observed and AM1 computed p(MIC) calculated for the pyrazolone compounds (Py1-Py7)under study for their antifungal activities on Colletotrichum falcatum (ITCC NO- 6656)



p(MIC) observed	p(MIC) calculated
-1	-0.961
-1	-1.092
-1	-1.103
-1.602	-1.227
-1	-1.144
-1.602	-1.66
-1.301	-1.318

Figure 4

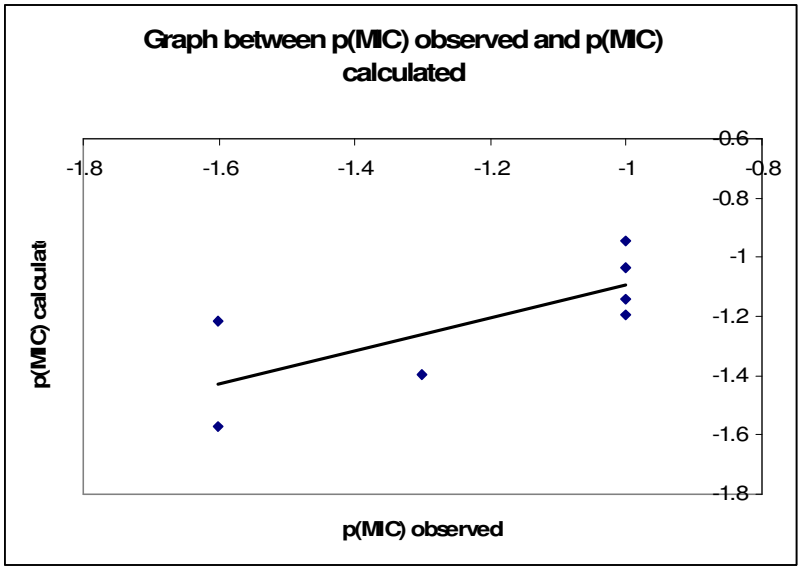
Trend line Graph between p(MIC) observed and PM3 computed p(MIC) calculated for the pyrazolone compounds (Py1-Py7)under study for their antifungal activities on Colletotrichum falcatum (ITCC NO- 6656)



p(MIC) observed	p(MIC) calculated
-1	-0.964
-1	-1.227
-1	-1.009
-1.602	-1.345
-1	-1.064
-1.602	-1.675
-1.301	-1.22

Figure 5

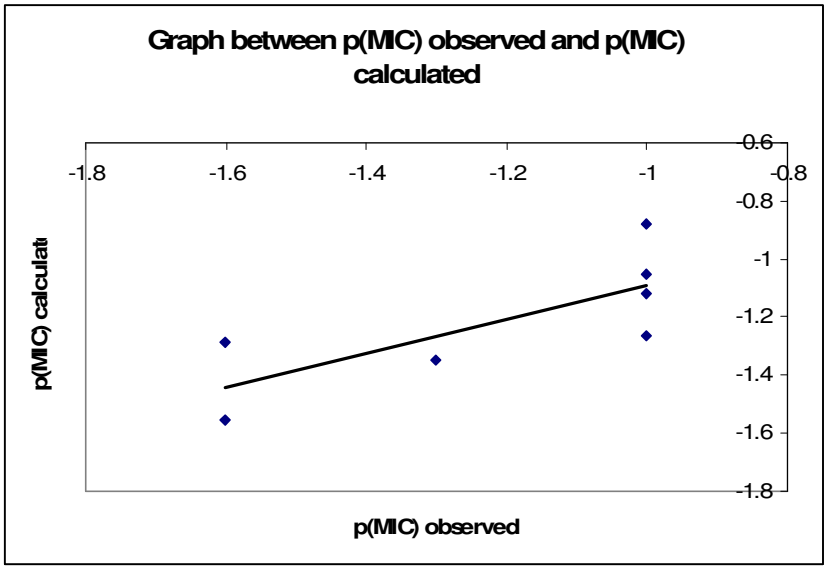
Trend line Graph between p(MIC) observed and MNDO computed p(MIC) calculated for the pyrazolone compounds (Py1-Py7)under study for their antifungal activities on Colletotrichum falcatum (ITCC NO- 6656)



p(MIC) observed	p(MIC) calculated
-1	-0.944
-1	-1.142
-1	-1.036
-1.602	-1.219
-1	-1.197
-1.602	-1.572
-1.301	-1.396

Figure 6

Trend line Graph between p(MIC) observed and ZINDO computed p(MIC) calculated for the pyrazolone compounds (Py1-Py7)under study for their antifungal activities on Colletotrichum falcatum (ITCC NO- 6656)



p(MIC) observed	p(MIC) calculated
-1	-1.117
-1	-1.055
-1	-0.88
-1.602	-1.287
-1	-1.263
-1.602	-1.556
-1.301	-1.347

CONCLUSION

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/ Pyrazolones (Py1-Py7)/ *Colletotrichum falcatum* (ITCC NO- 6656): - SAA, SAG and DM
PM3/ Pyrazolones (Py1-Py7)/ *Colletotrichum falcatum* (ITCC NO- 6656): - SAG,VOL and SAA
MNDO/ Pyrazolones (Py1-Py7)/ *Colletotrichum falcatum* (ITCC NO- 6656): - SAA, ZPE and HF
ZINDO/ Pyrazolones (Py1-Py7)/ *Colletotrichum falcatum* (ITCC NO- 6656)**: -** SAA, HF and ZPE
In conclusion this may be said that these parameters / descriptors have more impact on (MIC) over all other descriptors computed and reported.

ACKNOWLEDGEMENT

Author sincerely acknowledges M.P. Council of Science and Technology, Bhopal for financial assistance in the form of Research Project sanctioned to him. {Endlt. No. 6051/CST/R&D/2011 Dated 31-03-2011}

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