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Anticancer and antimicrobial activity of 3-Amino-2-mercapto quinazolin-4-one schiff bases and their VO(IV) and Pt(II) metal complexes

[1] Ramu Guda, [2] Srujana Muthadi, [3] Mahinder Porika and [1] Mamatha Kasula*.

[1] Department of Chemistry, Kakatiya University, Warangal, Telangana, India.

[2] University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana, India.

[3] Department of Biotechnology, Kakatiya University, Warangal, Telangana State, India.

* **Corresponding Author:** E-Mail: mamatakasula@gmail.com.

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ABSTRACT

A new series of bidentate mercapto quinazoline schiff bases, and their VO(IV) and Pt(II) complexes using 2-Hydroxy benzaldehyde, 2-Hydroxy naphthaldehyde, Pyridine-2-carbaxaldehyde and Thiophene-2-Carboxaldehyde has been synthesized and characterized by elemental analysis, magnetic, IR,^{1}H NMR and UV-VIS spectroscopy. The synthesized compounds were screened for their antimicrobial and cytotoxic activities against HeLa human cervical and MCF-7 breast cancer cell lines.

Keywords: Mercapto Quinazolines, Hydroxy and Non-hydroxy aldehydes, Mononuclear Complexes, Antimicrobial activity and Cytotoxic activity.

1. INTRODUCTION

Although several classes of anticancer and antimicrobial compounds are presently available, the resistance of microorganisms to these drugs has been constantly emerging. In order to address this serious medical problem, the medicinal chemists have focused their attention on organic compounds and natural products but not on metallo-organic entities in search of a new drug.

Quinazolines are bicylic compounds which play an important role in synthetic organic chemistry. Among quinazolines, particularly those which are C-2 and N-3 disubstituted quinazoline-(3H)-4-Ones are reported to be physiologically and pharmacologically active and find applications in the treatment of several diseases such as leprosy, mental disorders etc. These compounds have also been used as anti-bacterial, anti-fungal, anti-tubercular, anti-convulsant, anti-pyretic, anti-amoebic, anti-fertile and plant growth regulating agents [1-6]. In analytical chemistry quinazolines also find applications by acting as multidentate ligands [7] with metals usually from the transition group.

Schiff bases constitute an important class of organic compounds for which they are endowed with synthetic flexibility and can be obtained with varied substitutions widely by the selection of appropriate reactions. Furthermore, by changing the nature and the position of donor atoms or groups, it is possible to control the size of chelate rings formed and also helps to exploit the effect of substitution. These factors make schiff bases, with appropriate structure, chelating agents of great potential. In biological front, schiff bases serve as model compounds of several vitamins and enzymes [8-10]. These compounds have also been projected as promising pesticides, fungicides and bacteriocides [11,12]. In addition, they possess a wide spectrum of medicinal properties as they are active against tuberculosis, leprosy, viral infections and certain types of tumors[13-18] etc. Various studies have also shown that the azomethine group, having a lone pair of electrons in either a 'P' or 'SP^2' hybridized orbital on triagonally hybridized nitrogen has considerable biological importance. It was often been thought the biological activity of these compounds is due to their ability to chelate metal ions. The synthesis and characterization of metal complexes with bioactive organic ligands, particularly the schiff bases, is one among the promising fields for the research, as the metal ion association exerts a synergistic effect on the activity of the free ligands [19-21].

As the schiff base derivatives of quinazolines and their metal complexes play an

important role in many biological processes, and our earlier research work involved the synthesis, characterization, and bioactivity evaluation of quinazolyl based schiff bases [22-24] and their Mn(II), Fe(III), Co(II), Ni(II), Cu(II), Zn(II), Pd(II), Cd(II) and Hg(II) complexes, based on the encouraging results obtained with regard to the biological activity of these systems, through this paper, we report the synthesis and characterization of the ligand system obtained by the reaction of 2,3-disubtituted mercapto quinazoline with 2-hydroxy benzaldehyde (HBAMQ), 2-hydroxy naphthaldehyde (HNAMQ), Pyridine-2-carboxaldehyde (PMAMQ) and Thiophen-2-carboxaldehyde (TMAMQ) and their VO(IV) and Pt(II) complexes by physico-chemical methods(scheme-1) and also evaluate their antimicrobial activities against different types of bacterial, fungal species and also for their anticancer activity against HeLa Human cervical and MCF-7 breast cancer cell lines.

2. EXPRIMENTAL

2.1. Materials

All the chemicals used were AR and BDH grade. 3-Amino-2-mercapto-quinazoline-4-(3H)-ones (i) was prepared as reported earlier[25]. The ligands HBAMQ, HNAMQ, PMAMQ, and TMAMQ were synthesized by refluxing equimolar methanolic solutions of (i) and the respective aldehydes in presence of few drops of piperidine for 3 to 6 hours. The solids that separated during reflux were filtered, washed with methanol and recrystallized from hot dry methanol.

VO(IV) and Pt(II) complexes were prepared taking respective metal sulphates and metal chlorides. In the preparation of all the metal complexes, the metal and the ligands were combined in 1:1 or 1:2 mole ratio (the metal being in slight excess of what the ratio required) using required quantities of THF, DMSO, hot methanol and/or ethanol for the ligands and metal salts so as to effect their solubility. The contents were refluxed on a water bath for about 8-12 hours by maintaining the pH of the solution 8.2 - 9.5. The solid that separated was filtered, washed with water, hot methanol, ether and vaccum dried over $CaCl_2$.

The process of elemental analyses was carried out by Osmania University, Hyderabad. The magnetic studies of the metal complexes were recorded by using magnetic susceptibility meter MS_2G. Single frequency sensor Barington Company. The infrared spectra of the ligands and the metal complexes were recorded in KBr pellets in the range 4000-400 cm^{-1} on Perkin Elmer-BX spectrophotometer at Central Instrumentation Center, Kakatiya University, Warangal. The electronic spectra of the metal complexes in DMF were recorded on ELICO SL-159 UV-VIS spectrophotometer and systronics Double beam UV-VIS spectrophotometer: 2201 at chaitanya Degree and PG College, Hanamkonda, Warangal. ^{1}H-MR and 13C-NMR were recorded in CDCl3 and DMSO (Bruker Aspect AM-400 instrument) at 400/75 MHz respectively. The chemical Shift values (δ) are given in ppm). EI-MS spectra were recorded on a JMS-HX-110 spectrometer with a data system.

2.2. Synthesis of ligands

The reactions of aryl aldehydes like salicylaldehyde, 2-hydroxy naphthaldehyde, pyridine-2-carboxaldehyde and thiophene-2-carboxaldehyde (1mmole) with 3-amino-2-mercapto-quinazolin-4-one in the presence of few drops of piperidine as a base catalyst were carried out in methanol and refluxed on hot water bath for 3-6 hours. The crude products obtained were purified from methanol and recrystallized by hot dry methanol.

2.2.1. 3-(2'-Hydroxybezalamino)-2-mercapto-quinazolin-4-one (HBAMQ)

Yellow solid**,** yield (78%), M.P. 190 ^oC. Found % C, 60.26; H, 3.69; N, 14.02, $C_{15}H_{11}N_3O_2S$ requires % C, 60.59; H, 3.74; N, 14.14. IR (KBr) cm^{-1}: 3200 (NH), 3455 (OH), 1718 (C=O), 1583 (C=N). ^{1}H NMR (DMSO-d_6): 6.90-6.96 (m, 2H, Ar-H),7.21-7.30 (m, 2H, Ar-H),7.30-7.40 (d, 2H, Ar-H), 7.64-7.84 (m, 1H, Ar-H), 8.02 (d, 1H, Ar-H), 8.70 (s, 1H, N=CH), 11.43 (s, 1H,NH), 11.849 (s, 1H, OH). ^{13}C NMR (DMSO-d_6): 116.8, 117.8, 119.2, 119.6, 123.1, 124.4 125.7, 126.6, 130.2, 131.2, 134.7, 147.8, 148.2, 157.7, 161.6

2.2.2. 3-(2-Hydroxy-naphthalamino)-2-mercapto-quinazolin-4-one (HNAMQ)

Mustard yellow solid, yield (82%), M.P. 228^oC, Found % C, 65.39; H, 3.67; N, 11.98; $C_{19}H_{13}N_3O_2S$ requires % C, 65.68; H, 3.78; N, 12.10, IR(KBr) cm^{-1}: 3200 (NH), 3450 (OH),1718 (C=O), 1586 (C=N). ^{1}H NMR (DMSO-d_6): 7.24 -7.27 (m, 2H, Ar-H), 7.37-7.42 (m, 2H, Ar-H), 7.57-7.60 (t, 1H, Ar-H), 7.67-7.80 (t, 1H, Ar-H), 7.86-7.91 (m, 2H, Ar-H), 8.01-8.03 (d, 1H, Ar-H) 8.14-8.16 (d, 1H, Ar-H), 9.70(s, 1H, N=CH), 13.2 (s, 1H, OH) , 11.5(s, 1H, NH), ^{13}C NMR (DMSO-d_6): 109.3, 117.93, 119.56, 120.83,123.32, 123.90, 125.85, 126.64, 127.99, 128.20, 129.36, 132.12, 132.43, 134.84, 145.61, 148.18, 148.66, 157.95, 161.7.

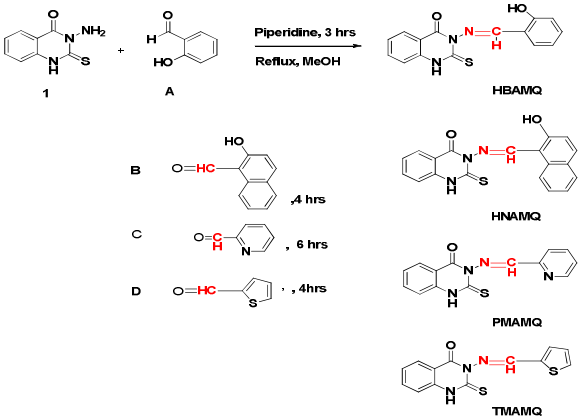
2.2.3. 3-(2'-Pyridylmethyleneamine)-2-mercapto-quinazolin-4-one (PMAMQ)

Light brown solid, yield (80%), M.P. 130^oC. Found % C, 59.37; H, 3.53; N, 19.69; $C_{14}H_{10}N_4OS$ requires % C, 59.55; H, 3.58; N, 19.85. IR(KBr) cm^{-1}: 3447 (NH), 1685 (C=O), 1584 (C=N).

^{1}H NMR (DMSO-d_6): 7.21-7.26 (m, 2H, Ar-H), 7.31-7.32 (m, 2H, Ar-H), 7.40-7.42 (d, 2H, Ar-H), 7.52-7.54 (m, 1H, Ar-H),7.94 (d, 1H, Ar-H), 8.72 (s, 1H, N=CH), 11.3 (s, 1H, NH); ^{13}C NMR(DMSO-d_6): 118.2, 123.4, 124.4, 125.8, 126.5, 134.6, 137.0, 137.1, 148.6 134.7, 149.0, 149.7, 152.2, 154.1, 161.6.

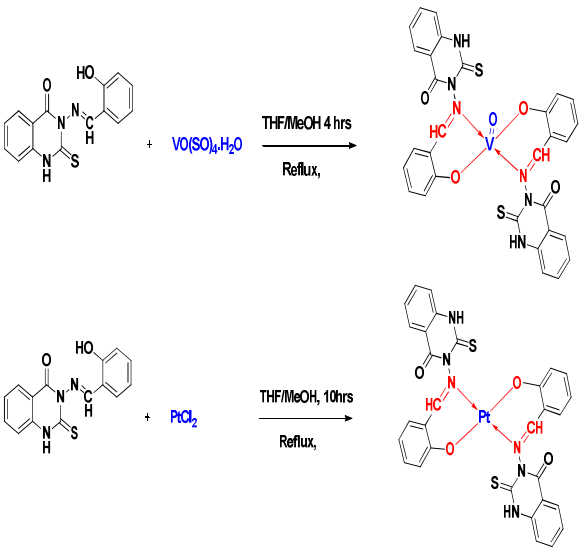
2.2.4. 3-(2'-Thienylmethyleneamino)-2-mercapto-quinazolin-4-one (TMAMQ)

White solid, Yield (81%), M.P. 140^{o}c, Found % C, 53.96; H, 3.03; N, 14.52; $C_{13}H_9N_3OS_2$ requires % C, 54.33; H, 3.16; N, 14.63. IR (KBr) cm^{-1}: 3447 (NH), 1685 (C=O), 1585 (C=N). ^{1}H NMR (DMSO-d_6): 7.02-7.10 (m, 2H, Ar-H), 7.12-7.14 (m, 2H, Ar-H), 7.24-7.36 (d, 1H, Ar-H), 7.54-7.60 (m, 1H, Ar-H), 7.72 (d, 1H, Ar-H), 8.15 (s, 1H, N=CH), 11.4(s, 1H, NH), ^{13}C NMR (DMSO-d_6): 113..7, 116.3, 122.7, 126.7, 128.2, 132.5, 133.90, 134.6 ,134.7, 138.8, 143.8, 148.7, 157.2. 81.



2.3. Synthesis of metal complexes

The reaction of optically active chiral schiff base ligands that contains potential donar sites viz, azomethine nitrogen, phenolic oxygen and carbonyl oxygen with different metal salts like VO(IV)SO_4, Pt(II)Cl_2 in 1:1 and 1:2 ratio yielded their respective complexes.



2.4. Antibacterial activity

The in vitro antibacterial activities of the ligands HBAMQ, HNAMQ, PMAMQ and TMAMQ and their VO(IV) and Pt(II) complexes were assayed with two concentrations (600 and 900 µg/ml) against six representative gram+ve bacteria (Bacillus substilis, Bacilius megaterium, Bacillus pumilus, staphylococcus aureus, enterobacter aerogens and streptococcus pyrogens) and four representative Gram-ve bacteria (Escherichia coli, Klebsiella pneumonia, Proteus vulgaris, Enterococcus faecalis) using broth dilution method recommended by National Committee for clinical laboratory standards. Bacteria were grown overnight in Luria-Bertani (LB) broth at 37^{o}C harvested by centrifugation and then washed twice with sterile distilled water. Stock solutions of the total compounds were dissolved in DMSO solvent. Each stock solution was diluted with standard broth method. The inhibition of microbial growth under standardized conditions was utilized to demonstrate antibacterial action of compound.

2.5. Antifungal activity

Invitro antifungal activites of the shiff base ligands their complexes were assayed against fungal organisms viz, Candiad albicans, Fusarium oxysporium, Drechslera halodes and colletrotrichum falcatum. The test organisms were grown for 48 hours at 25^{o}c YPD broth (1% yeast extract, 2% peptone and 2% dextrose) harvested by centrifugation and then washed with sterile distilled water. All the newly synthesized compounds were tested in 4 concentrations i.e. 300, 600, 900, and 1200 µg/ml. The fungal activity was determined by using Itrazole as standard.

2.6. Anticancer activity

The anticancer assay of the compounds at concentrations 10, 30, 60, and 90 µg/ml against MCF-7 human breast cancer cell lines and at concentrations 3, 10, 30 and 60 µg/ml against HeLa human cervical cancer cell lines, has been carried out.

Cell viability was measured by the MTT assay. MCF-7 cells were plated into a 96-well plate at a density of 1×10^4 cells/well. Cells are grown overnight in the full medium and then switched to the low serum media followed by exposure to test compounds or DMSO control. After the treatment with different concentrations of test compounds the cells were incubated with MTT (2.5 mg/ml) for 2 hours. The medium was then removed and 100 µl of DMSO was added into each cell to dissolve formazan crystals, the metabolite of MTT. After thorough mixing the plate was read 570 nm for "optical density" that is directly correlated

with cell quantity. The results were represented as percentage of cytotoxicity/viability. All the experiments were carried out in triplicate from the % of cytotoxicity the IC_{50} values were calculated.

3. RESULTS AND DISCUSSIONS

3.1. Elemental analysis

The analytical data presented in table 1 confirms the assigned composition of the ligand and the complex. It may be seen from the table that the experimental values are in fair agreement with the calculated ones.

Table-1: Results of Elemental analysis

Complex	M	C	N	S
$VO(HBAMQ\text{-}H)_2$	7.34 (7.92)	27.84 (28.01)	6.14 (6.53)	4.52 (4.97)
$VO(HNAMQ\text{-}H)_2$	6.23 (6.85)	30.53 (30.71)	5.24 (5.65)	4.10 (4.30)
$VO(PMAMQ)_2(SO_4)$	6.83 (7.00)	22.93 (23.12)	7.53 (7.70)	4.16 (4.40)
$VO(TMAMQ)_2(SO_4)$	6.93 (7.06)	21.33 (21.65)	5.43 (5.82)	8.53 (8.87)
$Pt(HBAMQ\text{-}H)_2$	24.34 (24.78)	22.18 (22.88)	5.03 (5.33)	3.88 (4.06)
$Pt(HNAMQ\text{-}H)_2$	21.52 (21.99)	25.43 (25.72)	4.42 (4.73)	3.28 (3.60)
$Pt(PMAMQ)_2Cl_2$	22.55 (23.06)	19.52 (19.87)	6.34 (6.62)	2.82 (3.06)
$Pt(TMAMQ)_2Cl_2$	23.01 (23.22)	18.18 (18.58)	4.83 (5.00)	7.32 (7.61)

3.2. Magnetic moment values

The room temperature magnetic moment data obtained for the present complexes reveals that, the magnetic moment values of VO(IV) complexes fall invariably in the range of 1.70-1.73 BM for the reason that the ligand field about the d^1 vanadium(IV) ion is strongly axial and the orbital contribution to the magnetic moment is quenched. Hence, magnetic moment values observed for the present VO(IV) complexes are in the range of 1.78–1.80 BM as expected for an unpaired electron spin, hence, found to be paramagnetic in nature. The magnetic moment values observed for Pt(II) complexes were found to be with no magnetic moment and hence it is diamagnetic in nature.

3.3. IR Spectra

The ligands HBAMQ, HNAMQ reveals a sharp band around 1718 cm^{-1} and the ligands PMAMQ, TMAMQ around 1680 cm^{-1} due to νC=O of quinazoline ring. This band appears unshifted in the metal complexes of HBAMQ and HNAMQ but it is lower shifted in the metal complexes of PMAMQ and TMAMQ suggesting non-involvement of the group in coordination [26] with respect to HBAMQ and HNAMQ and involvement of the same in coordination with respect to PMAMQ and TMAMQ. It is observed that, All the ligands donot reveal a band in the range 2600-2550 cm^{-1} due to νS-H indicating that this group has undergone tautomerism into thione form. Further, these ligands reveal bands corresponding to the thioamide (H-N-C=S) group. These bands remain unshifted in their complexes indicating non-involvement of 'S' in co-ordination.

Further, to report that the HBAMQ and HNAMQ record small intensity bands in the region 3455 – 3200 cm^{-1}, the one at higher frequency due νO-H and the other at lower frequency due to ν N-H. The higher frequency band corresponding νO-H disappears in their metal complexes indicating the involvement of 'O–hydroxy group in complexation through deprotonation, where as the the νN-H band persists at the same frequency in their complexes.

A medium intensity band seems to make its presence in all ligands around 1586 cm^{-1} due to ν C=N has been found lower shifted by about 30 cm^{-1} in all the complexes pointing out that the nitrogen of this group is involved in coordination. In the ligands HBAMQ, HNAMQ, the coordination through oxygen of phenolic group and nitrogen of azomethine group of the ligands in all the complexes is substantiated by the appearance of non ligand bands in the far infrared region around 500 and 400 cm^{-1} assignable respectively to νM-O and M-N vibrations.

In the ligands PMAMQ and TMAMQ small intensity bands appear at 1380 cm^{-1} due to νC-N (pyridine cyclic) at 780 cm^{-1} due to ν C-S (Thiophene cyclic) remain unshifted in their complexes suggesting non-involvement of 'N' and 'S' present in the ligands PMAMQ and TMAMQ in coordination. Based on all these observations it may be concluded that HBAMQ and HNAMQ ligands behave towards the metal ions as mononegative bidentate ligands coordinating through phenolic oxygen and azomethine nitrogen where as PMAMQ and TMAMQ behave towards the metal ions as neutral bidentate ligands coordinating through quinazoline carbonyl group and azomethine nitrogen.

3.4. Electronic Spectra

The UV-Visible spectra of all the complexes was obtained in methanolic solution. Each of the VO(IV) complexes of all the ligands show three peaks in their electronic spectra around 11,500-28,200 cm^{-1} which may be assigned respectively to the transitions $^2B_2 - {}^2E_2$, $^2B_2 - {}^2B_1$, and $^2B_2 - {}^1A_1$. Based on these observations and the analytical data and the other

data obtained it has been assigned square pyramidal geometry. The Pt(II) complexes of all the ligands each show three peaks in their electronic spectra around 23,500-36,700 cm^{-1} which may be assigned respectively to the spin allowed transitions $^1A_{1g}$ - $^1A_{2g}$, $^1A_{1g}$ - ^1E_g and $^1A_{1g}$ - $^1B_{1g}$ square planar geometry.

Based on these observations and the data obtained the VO(IV) and Pt(II) complexes have been assigned square pyramidal and square planar geometries.

Table - 2: The IR spectral data of the synthesized ligands and the Rh(III) and Pt(II)

Compound	ν N-H	ν O-H	ν C=O	ν C=N
HBAMQ	3200	3455	1718	1583
VO- HBAMQ	3200	---	1718	1522
Pt- HBAMQ	3200	---	1718	1517
HNAMQ	3200	3450	1718	1586
VO- HNAMQ	3200	---	1718	1560
Pt- HNAMQ	3200	---	1687	1560
PMAMQ	3447	---	1685	1584
VO-PMAMQ	3422	---	1625	1550
Pt-PMAMQ	3447	---	1654	1560
TMAMQ	3447	---	1685	1585
VO-TMAMQ	3422	---	1654	1560
Pt-TMAMQ	3422	---	1660	1560

3.5. Anti bacterial activity

The results of the antibacterial screening of the ligands and their metal complexes are incorporated in table 3. Based on the observations, it was revealed that the activity profiles of the ligands and their metal complexes screened against the microorganisms are varying as some of the compounds are active either significantly or marginally while others are not.

The results indicate that most of the compounds are ineffective in inhibiting the growth of gram +ve and gram –ve bacteria. Where the compounds are active, they exert relatively more activity on some species of gram +ve and on some species of gram -ve bacteria. All the ligands exert significant activity against the microorganism though in different level. The compounds VO- HBAMQ, Pt-TMAMQ and Pt-PMAMQ exert relatively good activity against more number of species, and selectively active against one or two strains.

3.6. Antifungal activity

All the prepared complexes showed good to moderate activity in which Pt-PMAMQ and Pt-TMAMQ showed better activity against maximum strains. Due to their polar nature and heterocyclic ring system these compounds exert good activity against certain species of fungi.

Table – 3: Results of Anti bacterial activity

Organism	Conc (µg/ml)	Name the compound and Zone of inhibition in (mm)								
		VOL1	VOL2	VOL3	VOL4	PtL1	PtL2	PtL3	PtL4	strd
E Coli	**600**	NA	NA	2.8	2.8	NA	1.5	NA	NA	3.0
	900	NA	NA	5.6	4.9	NA	3.0	NA	NA	6.1
P.vulgaris	**600**	1.8	1.5	4.8	3.2	1.6	4.0	2.5	2.0	8.9
	900	3.6	3.0	9.6	6.4	3.2	8.0	5.1	4.0	16.0
E.faecalis	**600**	4.1	3.8	2.5	1.2	4.8	3.0	NA	6.2	12.8
	900	8.2	7.6	5.0	2.4	8.9	6.0	NA	12.4	20.3
K.pneumonia	**600**	1.7	1.5	5.0	6.0	1.5	2.5	1.2	3.0	3.2
	900	2.4	3.0	10.2	12.1	3.0	5.0	2.4	6.0	6.5
E.aerogens	**600**	4.8	2.2	1.5	NA	2.8	5.2	6.2	4.8	4.4
	900	8.9	4.4	3.0	NA	5.6	10.4	12.4	9.6	8.7
B.subtilis	**600**	1.5	1.2	3.0	1.8	1.3	NA	4.8	1.2	8.4
	900	3.0	2.5	6.2	3.6	2.6	NA	8.9	2.4	16.2
B.mega therim	**600**	3.8	1.8	4.8	5.0	3.0	1.2	5.0	6.2	6.2
	900	7.6	3.6	8.9	10.2	6.0	2.4	10.1	12.4	12.8

B.pumilis	**600**	4.8	NA	2.5	3.0	1.8	3.2	NA	4.8	7.2
	900	9.6	NA	5.0	6.0	3.6	6.4	NA	9.6	14.5
Staph. Aureus	**600**	NA	3.5	4.8	1.2	3.6	4.8	1.2	NA	10.3
	900	NA	7.0	9.6	2.4	7.2	8.9	2.4	NA	20.0
Strept. Pyogens	**600**	5.0	1.2	2.5	3.0	1.8	2.4	2.0	1.2	8.1
	900	10.2	2.5	5.0	6.0	3.6	4.8	4.0	2.4	16.4

Standard: Streptomycin

Table - 4: Results of Antifungal activity

Organism	**Conc (µg/ml)**	**Name the compound and Zone of inhibition in (mm)**								
		VOL_1	**VOL_2**	**VOL_3**	**VOL_4**	**PtL1**	**PtL2**	**PtL3**	**PtL4**	**Strd**
Candida albicans	**300**	3.4	3.2	NA	2.8	2.9	2.9	5.2	4.5	2.6
	600	6.8	6.1	NA	5.7	5.0	5.5	9.5	7.0	5.3
	900	13.1	11.0	NA	11.1	9.2	11.0	16.2	13.8	12.0
	1200	26.1	20.6	NA	22.6	17.8	23.0	25.8	25.7	23.0
Fusarium oxysporium	**300**	5.1	3.5	3.9	5.2	3.1	NA	5.2	4.5	5.4
	600	9.5	7.1	7.1	9.5	6.2	NA	9.3	9.8	10.8
	900	16.1	15.2	16.6	17.2	11.8	NA	18.2	17.1	20.0
	1200	32.2	31.4	32.3	33.1	23.9	NA	35.8	33.2	34.3
Dreschleria Halides	**300**	3.3	NA	4.1	4.8	3.2	2.8	4.2	5.9	3.5
	600	6.4	NA	8.6	9.1	5.89	6.28	7.21	9.01	7.56
	900	13.2	NA	16.0	16.2	11.5	13.2	13.8	16.9	14.7
	1200	25.5	NA	29.8	31.3	23.4	25.1	23.2	29.0	27.3
Colletotrichum Falcatum	**300**	4.1	5.8	4.2	3.6	4.5	3.5	4.4	NA	4.4
	600	7.8	10.7	8.1	6.9	7.2	7.8	8.8	NA	9.3
	900	15.3	18.4	15.0	13.2	15.2	15.7	15.2	NA	18.2
	1200	30.2	34.8	30.3	28.1	31.8	29.9	31.3	NA	33.7

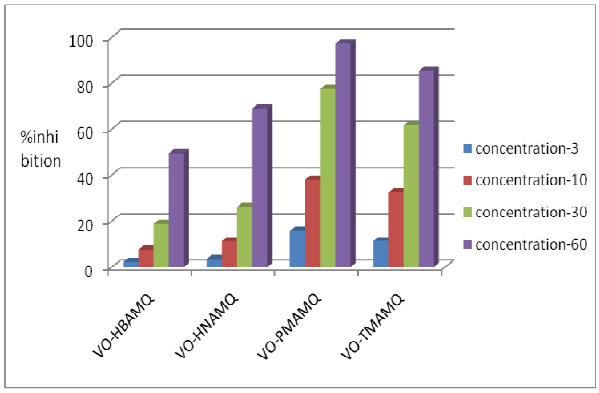
Standard: Itrazole

Table -5: IC50 values of VO(IV), Pt(II) metal complexes on MCF-7 and HeLa cell lines.

IC_{50} values on MCF-7 cell lines.		**IC_{50} values on HeLa cell lines.**	
Sample	IC_{50} value (µg/ml)	Sample	IC_{50} value (µg/ml)
VO-HBAMQ	80.2	VO-HBAMQ	63.7
VO-HNAMQ	45.7	VO-HNAMQ	45.6
VO-PMAMQ	20.4	VO-PMAMQ	21.3
VO-TMAMQ	29.3	VO-TMAMQ	27.6
Pt-HBAMQ	59.5	Pt-HBAMQ	57.2
Pt-HNAMQ	39.1	Pt-HNAMQ	50.2
Pt-PMAMQ	40.3	Pt-PMAMQ	39.7
Pt-TMAMQ	53.0	Pt-TMAMQ	44.1

Table – 6: Anti cancer activity of VO(IV) complex

Concentration (µg/ml)	% Inhibition			
	VO-HBAMQ	VO-HNAMQ	VO-PMAMQ	VO-TMAMQ
3	2.2	3.5	15.7	11.3
10	7.4	11.2	37.8	32.5
30	18.6	26.1	77.5	61.4
60	49.3	68.8	97.3	85.3

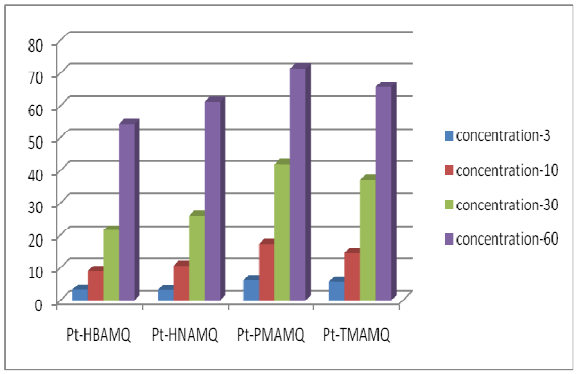


3.7. Anticancer activity

It was noticed that all the compounds exhibit differential effect with respect to their anticancer activity on the cell lines investigated. The compounds that have IC_{50} value less than 100 are considered significantly cytotoxic and the cytotoxicity of a compound increases as the IC_{50} values decreases. Among all the prepared complexes vanadyl complexes are found significantly cytotoxic on HeLa cell line and MCF–7 due to their low IC_{50} values than Pt(II) complexes.

Table – 7: Anti cancer activity of Pt(IV) complex

Concentration (µg/ml)	% Inhibition			
	Pt-HBAMQ	Pt-HNAMQ	Pt-PMAMQ	Pt-TMAMQ
3	3.1	3.0	6.1	5.6
10	8.9	10.5	17.3	14.6
30	21.5	25.8	41.8	37.1
60	54.2	61.1	71.3	65.7



4. CONCLUSION

In conclusion, the titled compounds were synthesized, characterized, and evaluated for antimicrobial and Cytotoxic studies against different species of microorganisms and HeLa Cervical, MCF-7 breast cancer cell lines. These compounds exhibited low to moderate activity against cancer cell lines. Among which Pt(II) complexes exhibited good microbial activity, whereas VO(IV) complexes exhibited good anticancer activity.

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