ejpmr, 2020,7(10), 714-722

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

ANTIBACTERIAL AND ANTIFUNGAL STUDIES OF CO(II), NI(II) AND ZN(II) COMPLEXES OF 6-PYRIDYL-5,6-DIHYDROBENZO[4,5]-IMIDAO[1,2-C] QUINAZOLINE (N-N)

Chaithra K.[1]*, H. G. Bheemanna[1] and V. Gayathri[2]

[1]Department of Chemistry, Vivekananda Institute of Technology, Bangalore-560074, India.
[2]Department of Chemistry, Central College Campus, Bangalore University, Bangalore –560 001, India.

***Corresponding Author: Chaithra K.**
Department of Chemistry, Vivekananda Institute of Technology, Bangalore-560074, India.
Email ID: chaithra.sudhi@gmail.com,

Article Received on 20/08/2020 **Article Revised on 09/09/2020** **Article Accepted on 30/09/2020**

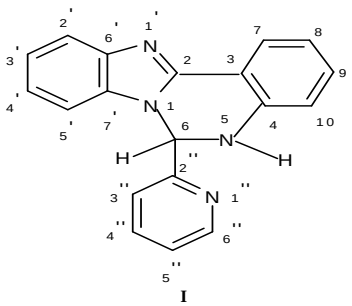
ABSTRACT

Cobalt(II), Nickel(II), and Zinc(II) salts react with a bidentate N-heterocycle, 6-pyridyl-5,6-dihydrobenzo[4,5]-imidao[1,2-C] quinazoline (N-N) to yield complexes of the composition MX_2(N-N). nH_2O (n = 0, M = Co, X = I or ClO_4; n =1, X = Cl or Br; n = 0, M = Ni, X = Br; n = 0, X = Cl or ClO_4; n = 0, M = Zn, X = Cl) and $[\{Zn(OClO_3)(N\text{-}N)_{1.5}\}ClO_4]_2$. The complexes are insoluble in common organic solvents but are soluble in dimethylformamide in which they behave as non-electrolytes excepting the chloro, bromo complexes of cobalt and the complex $[\{Zn(OClO_3)(N\text{-}N)_{1.5}\}ClO_4]_2$ which behave as uni-univalent electrolytes. The antimicrobial activity has been carried out using gram positive and gram-negative bacteria like Staphylococcus Aureus, Pseudomonas species, Bacillus species, E-Coli, Klebsiella at different concentration by Agar diffusion method and some fungus species like Aspergillus, Penicillium, Candida have been tested. The results are compared with the standard drug Amoxicillin 500 mg. The activity index was recorded using zone of inhibition.

KEYWORDS: Cobalt, nickel, zinc, quinazoline complexes, N-heterocycle, antimicrobial, antifungal, Agar diffusion.

1. INTRODUCTION

Quinazoline and its derivatives are widely known for their analgesic, antibacterial, antifungal, anti-convulsant, anti-inflammatory, anti-HIV, and anti-cancer activities, exhibited physiological and pharmacological interaction in targeting the receptors.[1-4] Herein, we describe the synthesis and characterization of the quinazoline ligand, 6-pyridyl-5,6dihydrobenzo[4,5]-imidao[1,2-C] quinazoline (I; N-N) and its reaction with cobalt, nickel and zinc halides and perchlorates. The synthesized ligand (I) was characterized by physical, spectral and single crystal x-ray structural analyses was reported.[5]



I

Bacterial resistance capacity increases with existing drugs due to enzyme susceptibility in their cell wall, the biological studies such as antimicrobial activity. These derivatives possess antibacterial activities especially against the gram-positive strains and with few fungal species by their interaction with the components present in cell wall and DNA molecules present in the nucleus.[6-8] Substitution of halogen atoms at 2, 6 and 8 positions showed the anti-microbial activity in addition to the substitution of $-CH_3$, $-NH_2$ group at position 3 and Thiol group at position 2. These substitutions are essential for biological assay of antimicrobial activity.[9]

2. MATERIALS AND METHODS

Experimental

Hydrated metal chlorides and metal bromides were procured from BDH. Metal iodide and hydrated perchlorates were prepared by dissolving metal carbonate in 1:1 or 1:2 aqueous hydroiodic acid and perchloric acid respectively and evaporating the resulting solution to almost dryness under reduced pressure. The N-heterocycle (I) was prepared following the procedure reported for related N- heterocycles.[10-12]

Measurements

C, H and N analyses of the complexes were carried out on a Heracus Carlo Erba 1108 microanalyser. Metal content was determined using a Spectra AA-30

spectrophotometer equipped with a Varian DS-15 computer. IR (nujol mull) spectra of the complexes were recorded on Shimadzu IR-435. Magnetic moment measurements at room temperature were made using a Gouy balance with $CuSO_4.5H_2O$ as the calibrant. Conductivity data were obtained using a Systronics –304 conductivity bridge. NMR spectra were recorded in DMSO–d_6 on AMX 400 MHz spectrometer using TMS as the internal standard at NMR Research centre I.I.Sc., Bangalore. TGA was carried out on a Mettler TAHE – 20 thermal analyzer with a scan rate of 5° C min^{-1} in air.

Preparation of the complexes

$CoX_2L.nH_2O$ (n = 1, X = I; n = 0, X = Cl or Br)

To a solution of hydrated cobalt(II)halide (1 mmol) in absolute alcohol/acetone-triethyl orthoformate(teof) mixture (10 cm^3), N-N (1 mmol) in absolute alcohol/acetone(10 cm^3) was added. The solution was refluxed for 4 hrs when a brown solid separated. The solid was washed with absolute alcohol/acetone and dried in vacuo. Yield: 70-80%.

$[Co(OClO_3)_2(N\text{-}N)]$

To a solution of hydrated cobalt(II) perchlorate (1 mmol) in absolute alcohol-teof mixture (10 cm^3), N-N (2 mmol) in absolute alcohol (10 cm^3) was added. The solution was refluxed for 5 hrs when a yellow solid separated. The solid was washed with absolute alcohol and dried in vacuo. Yield: 80%.

$NiX_2L.(H_2O)$ (n = 1, X = Cl; n = 0; X = I)

To a solution of hydrated nickel(II) halide (1 mmol) in absolute alcohol-teof mixture (10 cm^3), N-N (1 mmol) in absolute alcohol-teof mixture (10 cm^3) was added. The solution was refluxed for 5 hrs when a yellow solid separated. The solid was washed with absolute alcohol-teof and dried in vacuo. Yield: 80%.

$[Ni\ (N\text{-}N)_2(OClO_3)_2].H_2O$

To a solution of hydrated nickel(II) perchlorate (1 mmol) in absolute alcohol-teof mixture (10 cm^3), N-N (2 mmol) in absolute alcohol (10 cm^3) was added. The solution was refluxed for 5 hrs when a yellow solid separated. The solid was washed with absolute alcohol and dried in vacuo. Yield: 80%.

$[ZnCl_2\ (N\text{-}N)]$

To a solution of zinc(II) chloride (1 mmol) in ethanol-teof mixture (10 cm^3) was added slowly with stirring to 10 cm^3 of an ethanolic solution of the N-N (1 mmol) when a white precipitate separated out. The solid was washed with absolute alcohol and dried in vacuo. Yield: 80%.

$[\{Zn\ (OClO_3)\ (N\text{-}N)_{1.5}\}ClO_4]_2$

To a solution of zinc(II) perchlorate (1 mmol) in ethanol (20 cm^3) was added slowly with stirring an ethanolic solution (20 cm^3) of N-N (2 mmol) when a white solid precipitated out instantaneously. The mixture was allowed to stand at room temperature for about 1 hr and then the precipitate was washed with ethanol and dried in vacuo. Yield: 60%. Physical properties and analytical data of the complexes are listed in Table 1.

APPLICATION OF COMPLEXES

Antimicrobial activity

The most common methods were Agar well diffusion, Agar Plug diffusion, Cross streak, Poisoned food method and disk diffusion. Agar diffusion method was the best method to determine the Minimum Inhibitory Concentration (MIC) of antimicrobial substance.[20-22]

Preparation of Culture media

Nutrient Agar medium of composition Peptone (5 g), Beef extract (3 g) and Agar (15 g) in distilled water (1000 ml) at pH 6.8± 0.2 was used for the growth of microbes.

Standard drug

Amoxicillin is Penicillin antibiotic used to treat various bacterial and fungal infections like skin, bronchitis, Tonsillitis, Pneumonia, Urinary tract infections etc.[21]

Bacterial strains

As per the literature survey, Mycobacterium Smegmatis, M-Tuberculosis, M-Bovis, BCG, E-Coli were used for microbial growth on Agar, supplemented with Glycerol.[22]

Determination of Minimum Inhibitory Concentration (MIC)

MIC is the lowest concentration that prevent bacterial visible growth. Series of dilution were carried out to get particular concentration. At this concentration, inhibitory activity was determined. According to the literature survey, Ciprofloxacin was used as a standard drug against *streptococcus pyrogens*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *E-coli*.[23-26]

Herein, we studied the antimicrobial activity against *Bacillus Subtills*, *Staphylococcus aureus*, *Escherichia*, *Pseudomonas Vulgaris* and antifungal activity against pathogenic fungi i.e. *Aspergillus niger*, *Candida albicans*, which had shown the zone of inhibition for the above complexes at the concentration 1000 mg/mL [Complex (10 mg) in DMSO (10 ml)].[27-28]

Antibacterial Activity

In-vitro antibacterial activity was examined for the complexes and Amoxicillin-500 as standard). Antibacterial activities of the complexes against Gram-positive bacteria were investigated by the agar diffusion method. Further, the complexeswere used for the determination of zone of inhibition or sensitivity, against *Staphylococcus aureus* strain, *Bacillus Subtillis*, *E-coli*, *Pseudomonas aeruginosa*.

The antibacterial activity was performed on nutrient agar medium. The nutrient agar medium was prepared, autoclaved at 121^0C for 15 lbs, cooled and poured on

sterilized petriplates and solidified. After solidification, the complex and standard drug were introduced in different wells. The petriplates were incubated at 37^0C for 24 hours for the growth of bacteria. The zone of diameter was examined for the antibacterial activity[29-31] (Table3).

RESULTS AND DISCUSSION

The solid state i.r. spectra of the complexes are comparable with those of the uncoordinated N-heterocycle barring minor shifts in the positions of the peaks. The spectra of the complexes displayed peaks around 1535 and 1616 cm^{-1} due to $\nu_{C=C}$ and $\nu_{C=N}$ respectively and a peak at 3100 cm^{-1} due to the ν_{NH} vibration. The perchlorate complexes, in addition to the heterocycle peaks, showed additional peaks due to the perchlorate group. The perchlorate complexes of cobalt and nickel displayed split peaks around 1095 and 622 cm^{-1} which are characteristic of coordinated perchlorate group. The $[\{Zn(OClO_3)(N\text{-}N)_{1.5}\}ClO_4]_2$ complex exhibited peaks at 1119 and 633 cm^{-1} due to ionic perchlorate groups.[13]

The room temperature magnetic moments of the complexes indicate the paramagnetic nature of the metal ions. The magnetic moments of the chloro, bromo and perchlorate complexes of Co(II) are in the range 4.0 – 4.4 BM. The values are typical of tetrahedral geometry for the complexes. The $[CoI(N\text{-}N)_2]I$ complex has a magnetic moment of 4.9 BM and this is expected for a trigonal bipyramidal geometry. The μ_{eff} values of nickel (II) halo complexes are in the range 3.0 - 3.4 BM. The values are in the range expected for tetrahedral/square pyramidal geometry.[14-16] The μ_{eff} value of $[Ni(OClO_3)_2(N\text{-}N)_2]H_2O$ is 2.98 BM. The value is in the range expected for octahedral geometry. The electronic spectra of the complexes have been recorded in nujol mull. The spectra of cobalt(II) complexes exhibited three multiple absorption bands around 4000, 8000 and 16000 cm^{-1}. The positions of the bands and their intensities suggest a tetrahedral geometry for the complexes. The bands are assigned to the transitions $^4A_2 \rightarrow {}^4T_2(F)(\nu_1)$, $^4T_1(F)(\nu_2)$ and $^4T_1(P)(\nu_3)$ respectively. The electronic spectrum of $[Ni(OClO_3)_2(N\text{-}N)_2]H_2O$ has displayed bands of low intensity at 8291, 11737 and 28571 cm^{-1} and the bands are assigned respectively to the transitions $^3A_{2g}(F) \rightarrow {}^3T_{2g}$, $^3T_{1g}$, $^3T_{1g}(P)$. The bands are split and the nature of splitting indicates that the tetrahedral structure is distorted. The ligand field (10 Dq), the Racah (B', interelectronic repulsion) and nephelauxetic (β) parameters have been calculated for the complexes. The 10 Dq values for the halo complexes follow the known spectrochemical series order I < Br < Cl. The magnitude of B' in the complexes is considerably reduced relative to the free ion value (971 cm^{-1}) indicating appreciable covalent character for the metal–ligand bonds.

Table 1. Analytical data and IR Spectral data of the cobalt (II), nickel(II) and Zinc (II) complexes

Compound	Color	M.p (^{0}C)	μ^a_{eff} (BM)	Λ^b (Ω^{-1} cm^2 mol^{-1})	Analytical data Found (calculated. %)				I.r. Spectral data (cm^{-1})			[c] Transitions and assignments			[d] Crystal field parameters		
					Co/Ni/Cu	C	H	N	ν_{NH}	$\nu_{C=C}$ & $\nu_{C=N}$	ν_{ClO4}	$^4A_2(F) \rightarrow {}^4\nu(F)$	$^4A_2 \rightarrow T_1(F)$	$^4A_2 \rightarrow {}^4T_1(P)$	10dq	B'	β
(N-N)	White	230	-	-	-	77.00 (76.49)	4.73 (4.73)	18.32 (18.78)	3100	1545, 1616							
$[CoCl_2(N\text{-}N)]H_2O$	Brown	>250	4.2	28	12.60 (12.69)	49.25 (49.15)	4.00 (3.90)	12.10 (12.07)	3180	1535, 1610		4322	8250	15290	4105	668	0.687
$[CoBr(N\text{-}N)_2H_2O]Br$	Brown	> 250	4.0	83	11.00 (10.99)	42.59 (42.56)	2.95 (3.00)	10.55 (10.45)	3210	1536, 1600		4340	8291	15576	994	698	0.718
$[CoI(N\text{-}N)_2]I$	Brown	> 250	5.0	84	9.65 (9.64)	50.15 (50.18)	3.05 (3.10)	12.65 (12.70)	3225	1533, 1595		4766	6720	---	---	---	---
$[NiCl_2(N\text{-}N)]H_2O$	Yellow	>260	3.4	15	13.00 (13.16)	51.10 (51.17)	3.61 (3.61)	12.50 (15.56)	3180	1535, 1600		6720	10000	16820	5398	708	0.680
$[NiI_2(N\text{-}N)]$	Buff	>250	3.4	12	9.50 (9.60)	37.32 (37.35)	2.30 (2.31)	9.10 (9.17)	3210	1538, 1600		6313	8319	16725	6313	407	0.399
$[Ni(OClO_3)_2(N\text{-}N)_2]H_2O$	Yellow	>250	2.9	23	6.72 (6.72)	52.29 (52.31)	3.40 (3.46)	12.82 (12.84)	3240	1538, 1600	1079 (ν_3), 622 (ν_4)						
$[ZnCl_2(N\text{-}N)]$	Yellow	>260	---	4	15.00 (15.04)	52.63 (52.50)	3.27 (3.24)	12.90 (12.89)	3150	1533, 1605							
$[\{Zn(OClO_3)(N\text{-}N)_{1.5}\}ClO_4]_2$	Yellow	>260	--	86	9.12 (9.18)	48.08 (48.09)	2.98 (2.98)	11.75 (11.80)	3280	1543, 1626	1103 (ν_3), 633 (ν_4)						
$[Co(OClO_3)_2(N\text{-}N)]$	Brown	>250	4.4	25	10.49 (10.59)	41.20 (41.02)	2.50 (2.53)	10.10 (10.07)	3180	1538, 1600	1083 (ν_3), 628 (ν_4)	4516	7610	11764	3948	439	0.451

Gouy method [b] Molar conductance of ca. 10^{-3} M solution in DMF [c] Spectra recorded as Nujol mull [d] B is taken as 927 cm^{-1} for the free Co^{2+} ion & 1041 cm^{-1} Ni^{2+} ion

Thermogravimetric analyses of the chloro complexes of cobalt, nickel and $[Ni(OClO_3)_2(N\text{-}N)_2]H_2O$ revealed the presence of lattice water molecule, while the bromo complex of cobalt indicated the coordinated water molecule. The lattice water is lost below 100°C, the coordinated water is lost above 100°C (Table-2).[17]

Table 2. Thermogravimetric data of the complexes.

Complex	Temperature ^{0}C	Weight loss (%)*	Species loss
$[CoCl_2(N\text{-}N)]\ H_2O$	<100	4.96(4.9)	H_2O (lattice)
$[CoBr(N\text{-}N).H_2O]Br$	200	3.4(3.3)	H_2O (coordinated)
$[NiCl_2(N\text{-}N)]H_2O$	<100	4.0(3.6)	H H_2O (lattice)
$[Ni(OClO_3)_2(N\text{-}N)_2]\ H_2O$	<100	1.69(1.7)	H_2O (lattice)

*Calculated values are in parentheses

The ^{1}H n.m.r. spectra of the N-heterocycle N-N, $[ZnCl_2(N\text{-}N)]$ and $[\{Zn(OClO_3)(N\text{-}N)_{1.5}\}ClO_4]_2$ have revealed that the proton resonances of quinazoline ring unit have undergone –ve coordination induced shifts (c.i.s = $\delta_{complex} - \delta_{ligand}$) (upfield shift) on complexation while benzimidazole and pyridine ring units have undergone +ve c.i.s on complexation. The resonance due to NH of quinazoline unit is around 5.42 δ. On deuteration, this peak disappears confirming it is due to the proton of NH in the quinazoline unit. The spectra of the complexes have revealed the no resonances around 5.4 ppm indicated the disappearance of NH group in quinazoline unit. The resonance signal for the CH-proton of quinazoline group is around 7.72 ppm. According to Orellana et al,[18] the c.i.s arise due to electron donation from the ligand to the metal via the σ bond, metal electron π-back donation to the ligands, Vander Waals interaction and magnetic anisotropy of ring currents.

N-N--- [H – 7(7.64d), H – 8,9 (7.24m), H – 10 (7.32d), CH (7.72s), NH (5.4s), H-2' (7.16d), H-3' (7.06t), H – 4'(6.80t) H – 5'(6.83d), H – 3" (7.94d), H-4"(7.74t), H-5"(7.30t), H-6"(8.4d)]

$[ZnCl_2$ (N-N)]--[H –7(7.66d), H – 8,9 (7.22m), H – 10 (7.35d), CH (7.75s), NH (7.69s), H-2' (7.16d), H-3' (7.10t), H – 4'(6.80t) H – 5'(6.88d), H – 3" (7.94d), H-4"(7.77t), H-5"(7.30t), H-6"(8.45d)]

$[\{Zn\ (OClO_3)\ (N\text{-}N)_{1.5}\}ClO_4]_2$ ---[H –7(7.65d), H – 8,9 (7.22m), H – 10 (7.34d), CH (7.73s), NH (7.69s), H-2' (7.15d), H-3' (7.11t), H – 4'(6.80t) H – 5'(6.89d), H – 3" (7.95d), H-4"(7.77t), H-5"(7.30t), H-6"(8.45d)]

The ^{13}C NMR spectrum of the N-heterocycle exhibits ten signals in the range of δ 110.0 – 158.4 and peak due to CH is at δ 68.50. The assignments of the signals are made with the aid of off-resonance decoupled spectrum of the heterocycle and literature reports. The resonances due to carbon atoms in the coordinated heterocycle are shifted upfield. The coordination induced shifts, (c.i.s = δcomplex - δligand). The negative c.i.s may be attributed to greater metal-to-ligand π-back donation, where as positive c.i.s to ligand–to–metal σ -donation.[19]

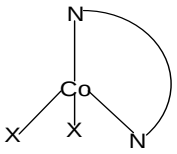
N-N—[C-2 (158.4), C-3(112.1), C-4(133.0), C-7(123.9), C-8(122.0), C-9 (122.2), C-10(124.6), CH(68.5), C-2'(110.4), C-3'(114.7), C-4'(118.1), C-5'(118.6), C-6'(142.9), C-7'(143.8), C-2"(146.9), C-3"(137.4), C-4"(120.2) C-5"(131.5), C-6"(149.64)]

$[ZnCl_2$ (N-N)]---[C-2 (158.32), C-3(112.0), C-4(132.99), C-7(123.94), C-8(122.1), C-9 (122.2), C-10(124.7), CH(68.43), C-2'(110.4), C-3'(114.74), C-4'(118.07), C-5'(118.56), C-6'(143.0), C-7'(143.7), C-2"(146.9), C-3"(137.4), C-4"(120.22) C-5"(131.59), C-6"(149.44)]

$[\{Zn(OClO_3)(N\text{-}N)_{1.5}\}ClO_4]_2$-----[C-2(158.36), C-3(112.08), C-4(133.05), C-7(123.92), C-8(122.103), C-9 (122.18), C-10(124.76), CH(68.5), C-2'(110.39), C-3'(114.75), C-4'(118.078), C-5'(118.57), C-6'(142.96), C-7'(143.84), C-2"(146.9), C-3"(137.39), C-4"(120.22) C-5"(131.54), C-6"(149.43)]

Stereochemistry

The analytical data, IR, NMR and electronic spectral results have indicated that the N-heterocycle is coordinated to the metal ion. The N-heterocycle is planar and can serve as chelating or bridging bidentate ligand. The complexes are proposed to have a tetrahedral geometry in which the N-heterocycle acts as a chelating bidentate ligand. The $[CoI(N\text{-}N)_2]I$, $[Ni(OClO_3)_2(N\text{-}N)_2]H_2O$ complexes are proposed to have trigonal bipyramidal/ octahedral geometries respectively.[13]

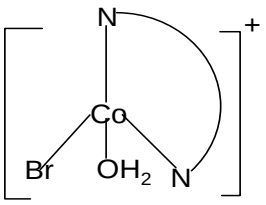


II

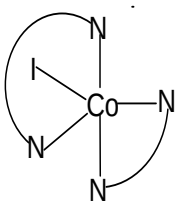
M = Co; X = Cl or ClO_4

M = Ni; X = Cl or I

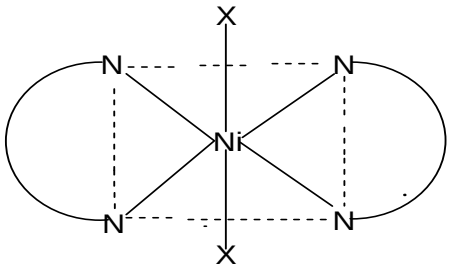
M = Zn; X = Cl



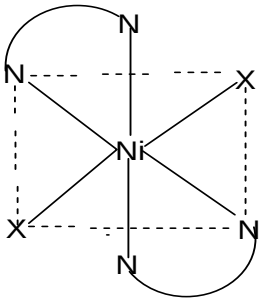
III



IV

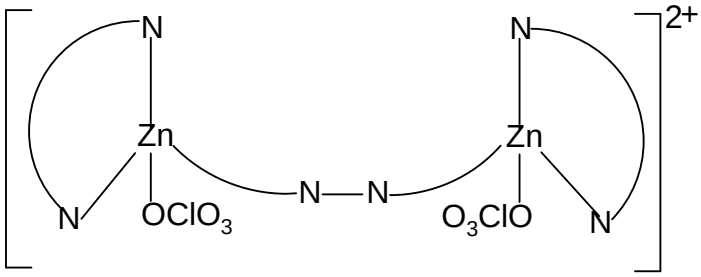


or



V

X = ClO_4



VI

Zone of inhibition

The zone of inhibition activity of the complexes was compared with Amoxicillin-500 (Fig 1-5) against *Staphylococcus aureus* and (Fig 6-10) against *Bacillus subtillis*.

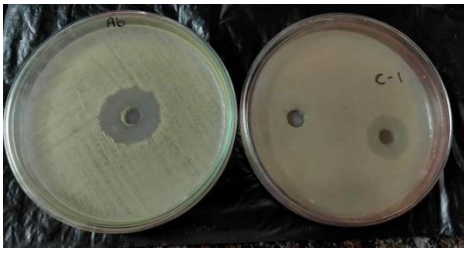


Fig 1: [$CoCl_2$ (N-N)] H_2O

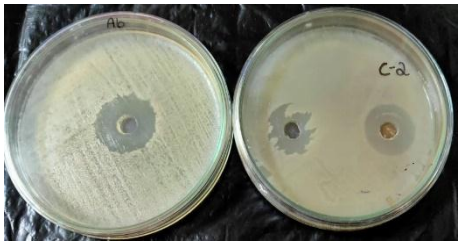


Fig 2: [CoBr(N-N).H_2O]Br

Fig3: [CoI(N-N)]I

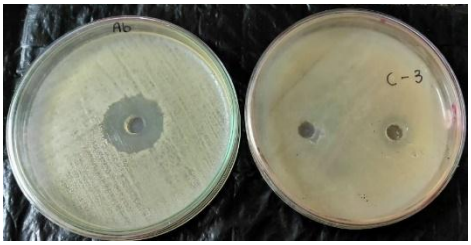


Fig 4: [$NiCl_2$ (N-N)]H_2O

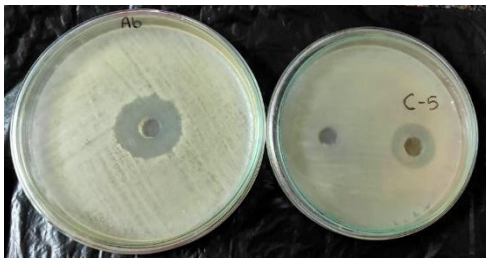


Fig5: [NiI_2 (N-N)]

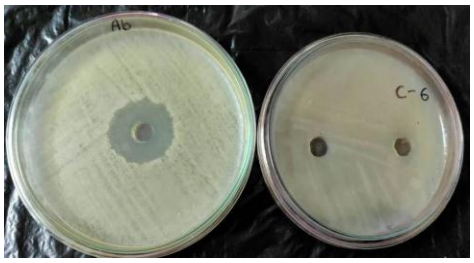


Fig 6:[$Ni(OClO_3)_2(N\text{-}N)_2$] H_2O

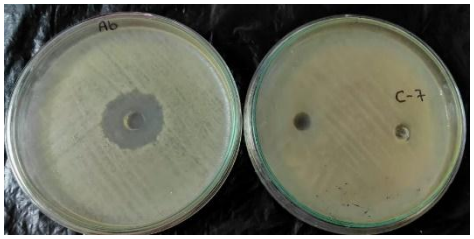


Fig 7: [$ZnCl_2$ (N-N)]

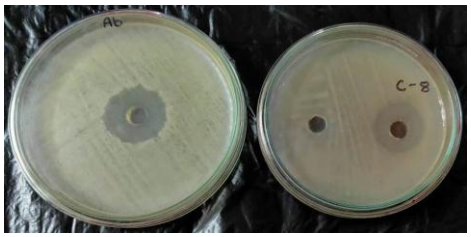


Fig 8: [{Zn ($OClO_3$) $(N\text{-}N)_{1.5}$}$ClO_4]_2$

Fig 9: [$Co(OClO_3)_2$ (N-N)]

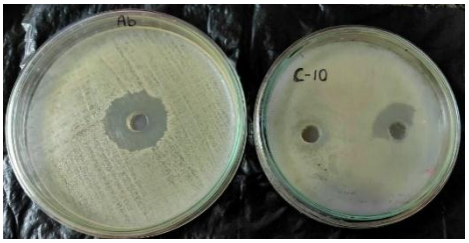


Fig 10: (N-N)

Table 3: Zone of diameter (antibacterial activity) of the complexes.

Complex	Zone of diameter (mm) at con. 150 mg	Zone of diameter (mm) at conc. 250 mg	Activity Index (%)
[$CoCl_2$ (N-N)] H_2O	6	1	60
[CoBr(N-N).H_2O]Br	9	3	90
[$CoI(N\text{-}N)_2$]I	1.5	0	15
[$NiCl_2$ (N-N)]H_2O	8	0	80
[NiI_2 (N-N)]	5	0	50
[$Ni(OClO_3)_2(N\text{-}N)_2$] H_2O	0	0	--
[$ZnCl_2$ (N-N)]	0	0	--
[{Zn ($OClO_3$) $(N\text{-}N)_{1.5}$}$ClO_4]_2$	7	2	70
[$Co(OClO_3)_2$ (N-N)]	2	2	20
(N-N)	3	2	30
Antibiotic (Amoxicillin-500)	10	10	100

$$\%Activity\ Index = \frac{Zone\ of\ inhibition\ of\ test\ compound}{Zone\ of\ inhibition\ by\ standard}\ X\ 100$$

Pseudomonas aeruginosa **E-coli**

Results revealed that *Staphylococcus aureus* shown maximum inhibition zone. The gram-negative bacterial species *E-Coli*, Pseudomonas *aeruginosa* shown negligible zone of inhibition.

Antifungal Activity

In-vitro antifungal activity was examined for the complexes of cobalt and nickel using Amoxicillin-500 as standard. The antifungal activity of the complexes against Penicillium strain was investigated by the agar diffusion method. Further, the complexes were used for the determination of zone of inhibition or sensitivity.[32-35]

The antifungal activity was performed on nutrient agar medium. The nutrient agar medium was prepared using Sabouraud Dextrose Agar (SDA) and autoclaved at 121^0C for 15 lbs, cooled and poured on sterilized petriplates and solidified. After solidification, the complex and standard drug were introduced in different wells. The petriplates were incubated at 28^0C for 72 hours for the growth of fungi. The zone of diameter was examined for the antifungal activity (Table 4).[36-38]

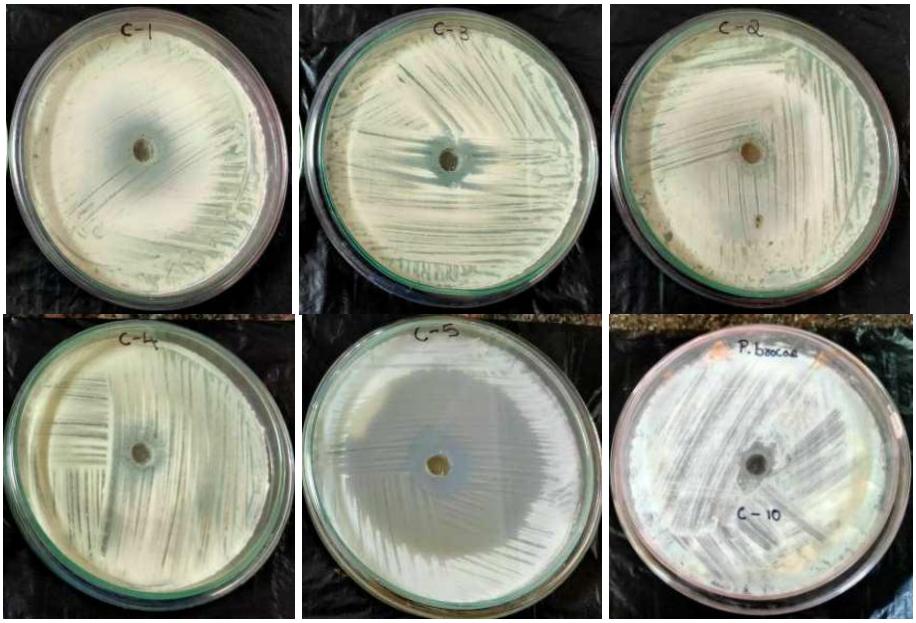


Table 4: Zone of diameter (antifungal activity) of the complexes.

Sl No	Complex [a]	Zone of diameter (mm)
1	*[$CoCl_2$ (N-N)] H_2O	0
2	[CoBr(N-N).H_2O]Br	3
3	*[CoI(N-N)]I	0
4	[$NiCl_2$ (N-N)]H_2O	2
5	[NiI_2 (N-N)]	6
6	(N-N)	2
7	Antibiotic (Amoxicillin-500)	10

- The concentration of sample - 250 mg/ml
- The concentration of Antibiotic- 100 mg/ml
- * No zone of inhibition

REFERENCES

1. N.S. Pawar, D.S. Dalal, S.R. Shimpi, P.P. Mahulikar∗, School of Chemical Sciences, North Maharashtra University, Jalgaon 425 001, India, European Journal of Pharmaceutical Sciences, 2004; 21: 115–118.
2. SaloniKakkar & Balasubramanian Narasimhan, BMC Chemistry volume 13, Article number, 2019; 16.
3. H.M. Al-Maqtari, J. Jamalis, T. Ben Hadda, M. Sankaranarayanan, S. Chander, N.A. Ahmad, H.M. Sirat, I.I. Althagafi, Y.N. Mabkhot, Res. Chem. Intermed., 2017; 43: 1893-1907.
4. M. Govindaraj, K. Vijayakumar, Vyshnavi N. Nair & Achsah V. Simon, International Journal of Engineering Research and Modern Education (IJERME) ISSN (Online): 2455-4200, 2016; I(I).
5. K. Jayalakshmi, H.C. Devaraje Gowda, Sridhar. M Anandalwar, H.G. Bheemanna, V. Gayathri, N.M.N. Gowda, Noor. S. Begaum, K.S. Rangappa and J.S. Prasad. Jap. Soc. Anal. Chem., 2004; 20: 88.
6. M. El Faydy, T. Djassinra, S. Haida, M. Rbaa, K. Ounine, A. Kribii, B. Lakhrissi, Mater. J. Environ. Sci., 2017; 8: 3855-3863.
7. Alexander Pöthig, Sara Ahmed, Hanne Cecilie Winther-Larsen, Shengyang Guan, Philipp J. Altmann, Jürgen Kudermann, Adriana Magalhães Santos Andresen, Tor Gjøen and Ove Alexander Høgmoen Åstrand, Front. Chem., 27 November 2018.
8. Archana Kapoor and NaiyaDhiman, Scholars Research Library Der Pharmacia Lettre., 2016; 8(12): 97-104.
9. PonmaniJeyakkumar, Ling Zhang, Srinivasa Rao Avula, Cheng-HeZhou, European Journal of Medicinal Chemistry, October 2016; 122(21): 205-215.
10. Mostafa Sayed, Adel M. Kamal El-Dean, Mostafa Ahmed & Reda Hassanien, Journal Synthetic Communications, An International Journal for Rapid Communication of Synthetic Organic Chemistry, 2018; 48: 4.
11. Devendra Singh Negi, Goutam Kumar, Mahender Singh and Navneet Singh, Journal of Chemistry, Published date: 04/09/2017.
12. Di Song, Prof. Shutao Ma, Med.Chem, April 5, 2016; 11(7): 646–659.
13. Bheemanna H G, Gayathri V and N M Nanje Gowda, IOSR Journal of applied Chemistry, e-ISSN; 2278-5736, April-2014; 7: 4.
14. P. Souza, J.A. Garcia-Vazquez and J.R. Masquer, Trans. met. Chem., 1984; **9:** 318.
15. R. Carballo, A. Castineirs, W. Hiller and J. Strahle, Polyhedron, 1993; **12:** 1083.
16. L. Bancia, A. Bencini, C. Benelli, D. Gatteschi and C. Zanchini, Structure and Bonding, 1982; **52:** 37.
17. Shivakumaraiah, N.M. Nanje Gowda, Ind. J. Chem., 2003; **42A:** 1860.
18. G.Orellana, C.A. Ibarra and J. Santoro, Inorg. Chem., 1988; **27:** 1025.
19. X. Xiaoming, Masa-aki-haga, T.M. Inoue, Yu Ru, A.W. Addision and K. Kano, J. Chem. Soc. Dalton Trans., 1993; 2477.
20. Zheng, MingZheng, XinLinga, YiLiu, YunshengXue, LinAn, NingGubMinJin, Bioorganic & Medicinal Chemistry Letters, 15 June 2013; 23(12): 3523-3530
21. R. Fleeman, Kurt S. Van Horn, Megan M. Barber, Whittney N. Burda, xDavid L. Flanigan, R. Manetsch, Lindsey N. Shawa, American Society for Microbiology, 6th, March 2017.
22. Nitesh Kumar Nandwana, Rajnish Prakash Singh, Om P. S. Patel, ShivDhiman, Hitesh Kumar Saini, Prabhat N. Jha, and Anil Kumar, ACS Omega, Nov 30, 2018; 3(11): 16338–16346.
23. Mohammad Asif, International Journal of Medicinal Chemistry, 2014; Article ID 395637, 27.
24. Bikui Tang, Meili Wei, Qun Niu, Yinjiu Huang, Shuo Ru, Xiaofen Liu, Lin Shen, and Qiang Fang, BioMed. Research International, 2017. Article ID 5791781
25. Kapoor, B., A. Nabi, R. Gupta, and M. Gupta, Asian Journal of Pharmaceutical and Clinical Research, Sept., 2017; 10(16): 7-12.
26. Ugale VG, Bari SB, 2014 Jun 10; 80: 447-501. doi: 10.1016/j.ejmech.2014.04.072. Epub, 2014 Apr 28.
27. R. Rohini, K. Shankar, P.M. Reddy, A. Hu and V. Ravinder. Europeon Journal of Medicinal Chemistry, 2010; 41: 1200.
28. Shatha Ibrahim Alaqeel, Journal of Saudi Chemical Society, 2017; 21: 229–237.
29. S. Frere, V. Thiery, C. Bailly and T. Besson. Tetrahedron, 2003; 59: 779.
30. V. Gayathri, N. Shashikala, N.M.N. Gowda and G.K.N. Reddy, Indian J. Chem., 1993; 32A: 33.
31. Ponmani Jeyakkumar, Ling Zhang, Srinivasa Rao Avula, Cheng-HeZhou, European Journal of Medicinal Chemistry, October, 2016; 122(21): 205-215.
32. ŞerefDemirayak, Gülşen A. Çiftçi, ŞafakUlusoylarYıldırım, Zafer A. Kaplancıklı, May, 2013; 346(5): 403–414. Arch Pharm.
33. S. Frere, V. Thiery, C. Bailly and T. Besson. Tetrahedron, 2003; 59: 779.

34. K.J. Akerman, C. Venter, L.A. Hunter and M.P. Akerman. J.Mol. Stru., 2015; 80: 1091.
35. H.G. Bheemanna, V. Gayathri, N.M.Nanje Gowda, J. Chem. Res., 2006; 530.
36. R. Walia1, Md. Hedaitullah, S. Farha Naaz, K. Iqbal and H S. Lamba, HIMT College of Pharmacy, Gr Noida, Uttar Pradesh, India., IJRPC, 2011; 1(3). Ramanpreet et al. ISSN: 22312781
37. Muthamuthu, ShameelaRajam, Christina Ruby Stella P., BharathiDileepan A. G. and R. Ranjith, Journal of Chemical and Pharmaceutical Research, 2016; 8(5): 505-526.
38. G.M. Higa and J. Abraham, Expert Review of Anticancer Therapy, 2007; 7: 1183.