

Macrocyclic divalent transition metal complexes of cobalt, nickel, copper and zinc with their antimicrobial, spectroscopic studies

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A series of tetra dentate macrocyclic metal complexes $[M(C_{16}H_{12}N_8)X_2]$ have been synthesized by template condensation of diaminomaleonitrile and diacetyl in presence of divalent metal ions where $M = Co^{II}, Ni^{II}, Cu^{II}, Zn^{II}$ and $X = Cl^{-1}, NO_3^{-1}, CH_3COO^{-1}$. Metal complexes are characterized by elemental analysis, conductance measurements, magnetic susceptibility measurements, IR, Far IR, NMR, ESR, electronic and mass spectra. Based on the molecular modeling studies and various spectral studies, distorted octahedral geometry has been proposed for metal complexes. All the complexes show low conductance values which indicate their non-electrolytic nature. Antimicrobial activities of macrocyclic complexes have been carried out *in vitro* against gram positive bacteria, gram negative bacteria and fungal strains showing good results as compare with standard drugs.

Keywords: Antimicrobial, Macrocyclic metal complexes, Octahedral geometry, Schiff base

In co-ordination chemistry, macrocyclic Schiff bases are broadly considered as stable and able to form complexes with vast variety of metals ions due to their admirable chelating properties¹. In current years, transition metal macrocyclic complexes have attracted attention as these are the active associate of metallo-enzymes² and bio-mimic model of complexes³. Further these complexes have much resemblance with natural proteins like Hemerythrin and enzymes. The macrocyclic complexes are much stable as compared to open chain complexes. Macrocyclic compounds have been widely used in detecting tumor lesions due to their chelating properties. Macrocyclic metal complexes also help in DNA nuclease activities as DNA modifying agents, which recognize and cleave the DNA^{4,5}. These complexes have chelating properties so they are used as chelating agents in chelating therapy as EDTA help in removing heavy metals. Recently the complexes of Diaminomaleonitrile ethylene diamine have gained much attention of the scientists because of their vast applications in various fields like dyeing material⁶, fluorescent light emitting devices⁷ in pharmacological studies⁸ and as DNA binding compounds⁹. Here we report, the synthesis and characterization of a new series of ten macrocyclic complexes resulting from diaminomaleonitrile and diacetyl, which have been

discussed in detail. The prepared complexes were tested for microbial efficacy.

Experimental Section

Material and physical measurements

All chemicals and solvents used were of analytical grade and used directly from sealed bottles. Transition metals salts were obtained from commercial resources. Diaminomaleonitrile and diacetyl were purchased from Sigma Aldrich, Fluka respectively. The IR spectra were recorded on Agilent technologies (carry 630) FT-IR spectrophotometer within the range 4000-400 cm^{-1} . The ¹H and ¹³C NMR spectra were measured at room temperature in DMSO-*d*₆ on Buckner AVANCE II 400 MHz NMR spectrophotometer with reference to Me₄Si. Electronic spectra were recorded on Hitachi 300 spectrophotometer. The microanalyses of C, H, and N were performed by elemental analyzer EUROEA (Model EA3000). The magnetic susceptibility measurements were performed on Vibrating Sample Magnetometer (Model PAR155). The conductivity of complexes was recorded on digital conductivity meter (HPG system, G-3001). Methods available in Literature were used to determine the quantitative analysis of metal in complexes¹⁰. All microbes were collected from Institute of Microbial Technology (IMTECH), Chandigarh.

The Agar-agar and malt yeast agar were used as culture medium for bacterial microbes and fungal microbes respectively. The studies of antibacterial, antifungal activities and minimum inhibitory concentration (MIC) were carried out and evaluated as per methods available in Literature¹¹.

Molecular modeling

3D Molecular modeling of proposed structure of metal complexes were performed using Avogadro 1.01 software program. This program was used to calculate the parameters like optimized energy, bond angle and bond length by molecular mechanics. For each molecule, several cycles of energy minimization had to be carried out.

Microbial studies

Based on clinical importance, six microbes were selected that are responsible for causing disease amongst human beings. The selected microbes were two Gram-positive bacteria (*Bacillus subtilis* (MTCC 8509), *Staphylococcus aureus* (MTCC3160)); two Gram-negative bacteria (*Escherichia coli* (MTCC 51), *Pseudomonas aeruginosa* (MTCC 2488)) and two fungi (*Candida albicans* (MTCC 3017) and *Saccharomyces cerevisiae* (MTCC 170)). These microbes were scrutinized for antibacterial and antifungal activities for synthesized complexes.

Synthesis of complexes

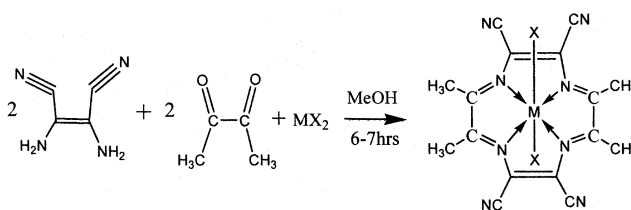
Template condensation reaction of diamines with diketones in presence of divalent transition metal salts has been represented by Scheme 1. A hot methanolic solution (20 cm³) of diaminomaleonitrile (2.5 mmol) was added to divalent metal salts of Co^{II}, Ni^{II}, Cu^{II} and Zn^{II} (1.25 mmol) dissolved in minimum quantity of methanol (20 cm³). The resulting mixture was refluxed for 1 h. Later methanolic solution of diacetyl was added to refluxing solution and constantly

refluxed for next 6-7 h at 60-72°C. The resulting solution was concentrated to half of its volume and kept in desiccator overnight. The resulting solution was cooled to room temperature. On cooling, overnight precipitates were formed which were vacuum filtered and washed sequentially with methanol, acetone and diethyl ether and finally dried at room temperature. The yield obtained was ~50-55%

Results and Discussion

Characterization and analysis

General properties and Chemical composition of complexes were determined by elemental analysis represented in Table 1. Macrocyclic complexes were found to be partially soluble in DMF and DMSO-d₆ solvent but insoluble in common organic solvents like benzene, toluene, chloroform, ethanol and methanol. Complexes were thermally stable up to ~270°C and started decomposing around ~600°C. According to analytical data, molecular formula of macrocyclic complexes is shown as [M (C₁₆H₁₂N₈) X₂]; where M = Co^{II}, Ni^{II}, Cu^{II}, Zn^{II} and X = Cl⁻, NO₃⁻, CH₃COO⁻. Dimensions of molar conductance of complexes in DMSO represent that these complexes have 1:1 electrolytes¹² having conductance of 11-25 Ω⁻¹ cm² mol⁻¹. Decomposition of complexes confirmed the positive



where M = Co (II), Ni(II), Cu(II), Zn(II) and X = Cl⁻, NO₃⁻, CH₃COO⁻.

Scheme 1 — Synthesis of metal Complexes derived from diaminomaleonitrile and diacetyl with divalent cobalt nickel copper and zinc metal salts.

Table 1 — Analytical data of synthesized Co(II), Ni(II), Cu(II) and Zn(II) complexes derived from diaminomaleonitrile and diacetyl

Sr. No	Complexes	Colour	\wedge_M	%M Found (Calcd)	%C Found (Calcd)	%H Found (Calcd)	%N Found (Calcd)	μ_{eff} B.M.
1	[Co(C ₁₆ H ₁₂ N ₈) Cl ₂]	Brown	21	13.16(13.22)	43.01(43.05)	2.65(2.69)	25.1(25.11)	4.02
2	[Co(C ₁₆ H ₁₂ N ₈)(NO ₃) ₂]	Brown	22	11.79(11.82)	43.00(43.05)	2.41(2.40)	22.4(22.44)	4.03
3	[Co(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	Dark brown	12	11.90(11.96)	41.04(42.60)	2.42(2.43)	22.6(22.71)	4.08
4	[Ni(C ₁₆ H ₁₂ N ₈) Cl ₂]	Orange	19	13.22(13.22)	38.04(38.40)	2.61(2.69)	25.1(25.11)	2.01
5	[Ni(C ₁₆ H ₁₂ N ₈)(NO ₃) ₂]	Brown	21	11.77(11.82)	37.99(38.90)	2.37(2.40)	22.41(22.44)	2.16
6	[Ni(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	Dark brown	16	11.95(11.96)	38.90(38.90)	2.41(2.43)	22.69(22.71)	2.20
7	[Cu(C ₁₆ H ₁₂ N ₈)Cl ₂]	Orange	11	14.02(14.09)	38.09(38.50)	2.63(2.66)	23.84(24.86)	1.98
8	[Cu(C ₁₆ H ₁₂ N ₈)(NO ₃) ₂]	Brown	20	12.61(12.61)	38.11(38.13)	2.34(2.38)	22.20(22.24)	1.78
9	[Cu(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	Brown	25	12.72(12.76)	38.92(38.94)	2.40(2.41)	22.51(22.51)	1.56
10.	[Zn(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	Dark brown	17	13.00(13.02)	38.43(38.47)	2.36(2.40)	22.43(22.44)	-

test for anions which specifies the presence of anions in coordination sphere in the chelates.

IR spectra

In IR spectrum of macrocyclic complexes, showed absence of characteristic band of carbonyl ν ($>C=O$) moiety of diacetyl at ν 1700 cm^{-1} and free amine group at $3200\text{-}3439\text{ cm}^{-1}$ suggesting the formation of macrocyclic framework. Appearance of absorption band near $1580\text{-}1615\text{ cm}^{-1}$ confirmed condensation of carbonyl group of diacetyl and amino group of diaminomaleonitrile. Lower value of frequency (ν) ($C=N$) group indicate the drift of lone pair density of azomethine nitrogen towards the metal ions¹³. In all the complexes, presence of bands near 2230 cm^{-1} (m) and 2196 cm^{-1} (vw) (characteristic of a nitrile group) rule out the possibility of coordination of nitrile group to metal ion¹⁴ (Fig. 1). IR spectra of all the nitrate complexes indicated that the two nitrate groups display the three (N–O) stretching bands at ν $1410\text{-}1455\text{ cm}^{-1}$ (ν_5), $1305\text{-}1315\text{ cm}^{-1}$ (ν_1) and $1015\text{-}1030\text{ cm}^{-1}$ (ν_2). The separation of two highest frequency bands ($\nu_5 - \nu_1$) suggested that both the nitrate groups are coordinated in unidentate manner¹⁵. All the acetate complexes show two bands at frequency $1630\text{-}1640\text{ cm}^{-1}$ (ν_1) and $1380\text{-}1390\text{ cm}^{-1}$ (ν_2) which indicate that acetate group is coordinated and acting as unidentate ligand¹⁶ (Fig. 1).

Far IR

In Far IR spectra, all the metal complexes showed bands in the region ($420\text{-}450\text{ cm}^{-1}$) related to the frequency bands (M–N) vibration¹⁷. The presence of these bands symbolizes the coordination bonding of azomethine nitrogen towards metal ions¹⁸. The presence of bands in the range $\sim 300\text{-}320\text{ cm}^{-1}$ may be due to the (M–Cl) vibration. The bands present in the range $\sim 220\text{-}270\text{ cm}^{-1}$ in all the nitrate complexes were assigned to (ν) (M–O) stretching vibrations.

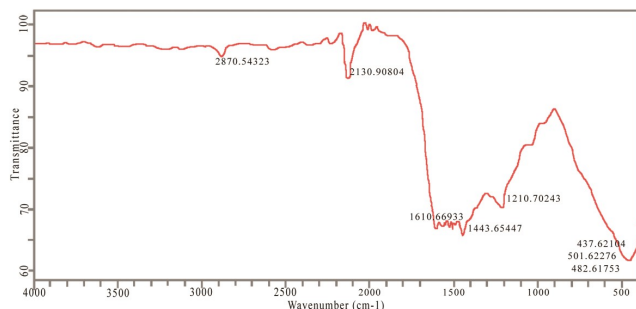


Fig. 1 — IR spectrum of $[Ni(C_{16}H_{12}N_{10})Cl_2]$.

1H NMR and ^{13}C NMR

The 1H NMR spectrum of the macrocyclic zinc (II) complexes $[M(C_{16}H_{12}N_8)X_2]$: exhibits singlet at 1.202 ppm region which corresponds to equivalent methyl protons of diacetyl. In ^{13}C NMR spectrum of Zn^{II} complex, TMS was used as internal reference and DMSO as solvent at ambient temperature. The chemical shift at 178 ppm in ^{13}C spectrum represents the presence of azomethine ($C=N$) carbon. The shift of diacetyl carbon appears at 18.7 ppm . The shift of nitrile carbon ($C\equiv N$) appears at 117.1 ppm .

Electronic Spectra

Magnetic moments of all the Co^{II} complexes were in the range $4.02\text{-}4.08\text{ B.M.}$ at room temperature. Electronic spectra of Co^{II} were observed in DMSO show the three absorption peaks in range (ν_1) $9010\text{-}9101\text{ cm}^{-1}$, (ν_2) $15130\text{-}16120\text{ cm}^{-1}$, (ν_3) $20690\text{-}21030\text{ cm}^{-1}$. The above spectra bear a resemblance to those complexes which are reported to have an octahedral geometry. Thus, we imagine effective symmetry to be D_{4h} instead of idealized O_h around the Co^{II} metal ions. The various bands allocated to the transitions are as follows: $^4T_{1g} \rightarrow ^4T_{2g}$ (F) (ν_1), $^4T_{1g} \rightarrow ^4A_{2g}$ (F) (ν_2), $^4T_{1g} \rightarrow ^4T_{1g}$ (P) (ν_3) respectively.

Ni^{II} complexes showed magnetic moments in the range $2.01\text{-}2.20\text{ B.M.}$ at room temperature. Electronic spectra of Ni^{II} complexes were observed in DMSO show three absorption peaks in the range (ν_1) $10260\text{-}11530\text{ cm}^{-1}$, (ν_2) $14580\text{-}16928\text{ cm}^{-1}$, (ν_3) $25012\text{-}25890\text{ cm}^{-1}$ respectively. The spectra were consistent with those complexes which are reported to have an octahedral geometry¹⁹. At ground state, octahedral coordinate of Ni^{II} were $^3A_{2g}$. So, these bands exhibits three spin transitions that would be $^3A_{2g}$ (F) \rightarrow $^3T_{2g}$ (F), $^3A_{2g}$ (F) \rightarrow $^3T_{1g}$ (F) and $^3A_{2g}$ (F) \rightarrow $^3T_{1g}$ (P) respectively. Thus, we assume the effective symmetry to be D_{4h} and not idealized O_h .

Magnetic moment of copper complexes were found in the range $1.78\text{-}1.98\text{ B.M.}$ Cu^{II} complexes shows two absorption bands in the region at $23320\text{-}29320\text{ cm}^{-1}$ with shoulder on low energy side at $10310\text{-}16340\text{ cm}^{-1}$. The spectra show that these complexes are distorted octahedral geometry. The sequence of d-orbital energy level for these complexes may be: $x^2-y^2 > z^2 > xy > xz > yz$, thus assuming the tetragonal distortion in the molecule. The broad band assigned to transitions were: $d_{xz}, yz \rightarrow d_{x^2-y^2}$ ($^2B_{1g} \rightarrow ^2A_{2g}$); $d_{xy} \rightarrow d_{x^2-y^2}$ ($^2B_{1g} \rightarrow ^2E_g$) and shoulder assigned to $d_z^2 \rightarrow d_{x^2-y^2}$ ($^2B_{1g} \rightarrow ^2B_{2g}$)²⁰. The strong high-energy frequency bands were assigned to metal \rightarrow ligand charge transfer.

The ligand field parameters like ligand field splitting energy $10Dq$, Racah inter-electronic repulsion parameter B , covalency factor β have been calculated and represented in Table 2. The value of covalency factor β accounts for the covalent nature of these complexes²¹.

ESR spectra

The ESR spectra of all the Cu^{II} complexes provide the beneficial information about the metal ion environment. The X-band ESR spectra of Cu^{II} complexes were examined in DMSO at room temperature. The ESR Spectra of $[\text{Cu}(\text{C}_{16}\text{H}_{12}\text{N}_8)\text{Cl}_2]$ exhibited an intense broad isotropic signal, without any hyperfine splitting, with $g_{\text{iso}} = 2.135$. The g_{iso} value (2.135) obtained from spectrum was compared to the g value of a free electron (2.0023), which indicated covalent nature of bonding between the metal ion and the ligands molecule²². Greater value of g_{iso} confirms the octahedral geometry around the central metal ion. This also accounts for exchange interaction between copper centers in adjoining molecules and purely dipolar in nature^{23,24}.

Mass spectra

The mass spectra have been very useful in determining molecular weight of macrocyclic metal complexes. The mass spectra of cobalt (II), nickel (II), copper (II), and zinc (II) complexes have been recorded and all complexes exhibit parent peaks due to molecular $[\text{M}]^+$ and $[\text{M}+2]^+$ ions. The mass spectrum of cobalt (II) complex (as shown in Fig. 2) exhibits molecular ion peak $[\text{Co}(\text{C}_{16}\text{H}_{12}\text{N}_8)\text{Cl}_2]^+$ at m/z 445.01 amu. The molecular ion peak for all the other complexes were as follows: $[\text{Co}(\text{C}_{16}\text{H}_{12}\text{N}_8)(\text{NO}_3)_2]^+$ at m/z 483 amu, $[\text{Co}(\text{C}_{16}\text{H}_{12}\text{N}_8)(\text{OAc})_2]$ at m/z 491, $[\text{Ni}(\text{C}_{16}\text{H}_{12}\text{N}_8)\text{Cl}_2]$ at m/z 445.6 amu, $[\text{Ni}(\text{C}_{16}\text{H}_{12}\text{N}_8)(\text{NO}_3)_2]$ at m/z 482 amu; $[\text{Ni}(\text{C}_{16}\text{H}_{12}\text{N}_8)(\text{OAc})_2]$ at 491 amu, $[\text{Cu}(\text{C}_{16}\text{H}_{12}\text{N}_8)\text{Cl}_2]$ at 449 amu, $[\text{Cu}(\text{C}_{16}\text{H}_{12}\text{N}_8)(\text{NO}_3)_2]$ at 502 amu, $[\text{Cu}(\text{C}_{16}\text{H}_{12}\text{N}_8)(\text{OAc})_2]$

at 516 amu, $[\text{Zn}(\text{C}_{16}\text{H}_{12}\text{N}_8)(\text{OAc})_2]$ at 636 amu. while comparing molecular formula weight with m/z values, it was found that suggested molecular formula were in perfect concordance with observed data for these complexes $[\text{M}(\text{C}_{16}\text{H}_{12}\text{N}_8)\text{X}_2]$ and confirm the formation of macrocyclic skeleton. Moreover, spectra also exhibited the various fragments obtained due to thermal cleavage.

Molecular modeling

Molecular modeling of the macrocyclic complexes were performed by using Avogadro 1.01. It helped to establish the structural features like effect on bond angles, bond length after coordination of metal ions towards coordination sphere. Considering these facts, the complexes of cobalt and copper were modeled and energy minimization had been carried out for each molecule in various cycles for calculating overall minimum energy. The root mean square gradient for the molecules was all less than one.

The $[\text{Co}(\text{C}_{16}\text{H}_{12}\text{N}_8)\text{Cl}_2]$ complex had distorted octahedral geometry with auto optimized energy 1763 kJ/mol and four nitrogen atoms are present at equatorial position. Co (II) ion lies on mean position of equatorial plane of four nitrogen donor atom. The equatorial Co (II)–N distance being 1.24° \AA and chloride ions occupy axial positions. The axial Co

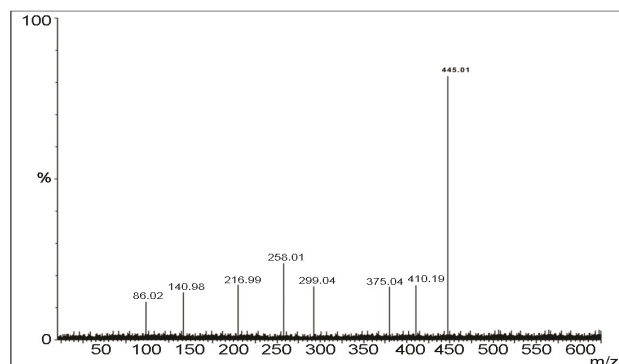


Fig. 2 — ^1H NMR spectrum of $[\text{Zn}(\text{C}_{16}\text{H}_{12}\text{N}_{10})(\text{OAc})_2]$.

Table 2 — Magnetic moment, electronic spectra and ligand field parameters

Sr. No	Complexes	λ_{max} (cm^{-1})	$Dq(\text{cm}^{-1})$	$B(\text{cm}^{-1})$	β	μ_{eff} B.M.
1	$[\text{Co}(\text{L})\text{Cl}_2]$	9010,16080,20690	707	700	0.72	4.02
2	$[\text{Co}(\text{L})(\text{NO}_3)_2]$	9101,15130,21030	603	589	0.62	4.04
3	$[\text{Co}(\text{L})(\text{OAc})_2]$	9060,16120,20789	706	649	0.66	4.08
4	$[\text{Ni}(\text{L})\text{Cl}_2]$	10420,15020,25012	1042	565	0.54	2.18
5	$[\text{Ni}(\text{L})(\text{NO}_3)_2]$	10260,14580,25890	1026	526	0.50	2.01
6	$[\text{Ni}(\text{L})(\text{OAc})_2]$	11530,16928,25632	1153	531	0.51	2.20
7	$[\text{Cu}(\text{L})\text{Cl}_2]$	10310,23320	-	-	-	1.78
8	$[\text{Cu}(\text{L})(\text{NO}_3)_2]$	16340,29320	-	-	-	1.98
9	$[\text{Cu}(\text{L})(\text{OAc})_2]$	10124,23670	-	-	-	1.82

Where $\text{L} = \text{C}_{16}\text{H}_{12}\text{N}_8$

(II)–Cl distance is 1.15° Å and 1.16° Å. Geometry optimized structure was shown in Fig. 3.

Optimized energy for copper complex [Cu(C₁₆H₁₂N₈)Cl₂] was found to be 714.7 kJ/mol. As a consequence of coordination between metal and donor atoms, the bond angles were distorted to some extent; bond angles Cl(27)–Cu(25)–Cl(26) and N(15)–Cu(25)–N(16) were 179.72° and 90.30°, respectively and indicated distortion in the geometry to small extent. All the bond angles and bond lengths were nearly equal to the octahedral geometry²⁵.

Microbial activities

The transition metal complexes have been tested for their antimicrobial activity against the bacterial species i.e. *Bacillus subtilis* (MTCC 8509), *Staphylococcus aureus* (MTCC 3160), *Escherichia coli* (MTCC 51), *Pseudomonas aeruginosa* (MTCC 2488).

The antifungal activities of the metal complexes have been examined on two yeast i.e. *Candida albicans* (MTCC 3017) and *Saccharomyces cerevisiae* (MTCC 170) by using agar well diffusion methods. *In-vitro* antimicrobial activities of the complexes are given in Tables 3, 4 and Fig. 4. The antibacterial and

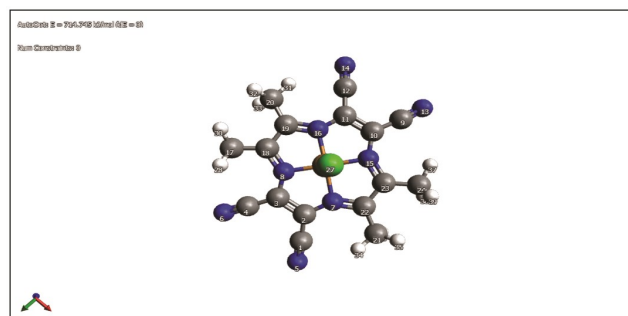


Fig. 3 — ¹³C NMR spectrum of [Zn(C₁₆H₁₂N₁₀)(OAc)₂].

Table 3 — In-vitro antimicrobial activity of synthesized macrocyclic metal complexes by using agar well diffusion method

Compound No.	Diameter of growth of inhibition zone (mm) ^a					
	Gram positive bacteria		Gram negative bacteria		Fungi	
	<i>Bacillus subtilis</i>	<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>	<i>Pseudomonas aeruginosa</i>	<i>Candida albicans</i>	<i>Saccharomyces cerevisiae</i>
[Co(C ₁₆ H ₁₂ N ₈)Cl ₂]	18	18	21	18	24	23
[Co(C ₁₆ H ₁₂ N ₈)(NO ₃) ₂]	16	23	22	20	28	22
[Co(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	-	-	18	20	22	24
[Ni(C ₁₆ H ₁₂ N ₈)Cl ₂]	20	18	18	22	22	21
[Ni(C ₁₆ H ₁₂ N ₈)(NO ₃) ₂]	18	18	17	18	18	20
[Ni(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	20	16	19	-	18	22
[Cu(C ₁₆ H ₁₂ N ₈)Cl ₂]	18	16	21	18	30	24
[Cu(C ₁₆ H ₁₂ N ₈)(NO ₃) ₂]	21	21	18	22	21	23
[Cu(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	21	23	18	22	25	24
[Zn(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	24	23	21	23	20	26
Ciprofloxacin	24.0	26.6	25.0	22	-	-
Amphotericin-B	-	-	-	-	16.6	19.3

Table 4 — Minimum inhibitory concentration of metal complexes

S. No	Compound No.	Gram positive bacteria		Gram negative bacteria		Fungi	
		<i>Bacillus subtilis</i>	<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>	<i>Pseudomonas aeruginosa</i>	<i>Candida albicans</i>	<i>Saccharomyces cerevisiae</i>
1	[Co(C ₁₆ H ₁₂ N ₈)Cl ₂]	5	25	NA	25	25	NA
2	[Co(C ₁₆ H ₁₂ N ₈)(NO ₃) ₂]	16	18	25	25	12.5	25
3	[Co(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	50	25	NA	25	25	Nt
4	[Ni(C ₁₆ H ₁₂ N ₈)Cl ₂]	25	50	50	25	25	25
5	[Ni(C ₁₆ H ₁₂ N ₈)(NO ₃) ₂]	7	5	-	16	50	25
6	[Ni(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	7	7	-	12.5	12.5	12.5
7	[Cu(C ₁₆ H ₁₂ N ₈)Cl ₂]	50	50	25	50	6.25	25
8	[Cu(C ₁₆ H ₁₂ N ₈)(NO ₃) ₂]	16	15	50	25	25	25
9	[Cu(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	9	14	7	10.5	12.5	25
10	[Zn(C ₁₆ H ₁₂ N ₈)(OAc) ₂]	25	25	25	25	25	12.5
	Ciprofloxacin	6.25	6.25	6.25	12.5	-	-
	Amphotericin-B	-	-	-	-	12.5	12.5

nt - Not tested; -: No activity

^a Values, including diameter of the well (8mm), are means of three replicates

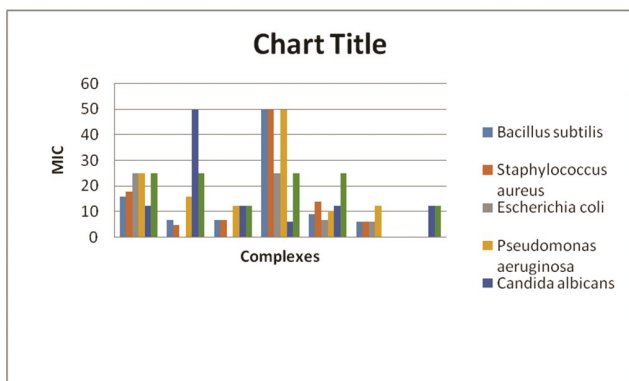
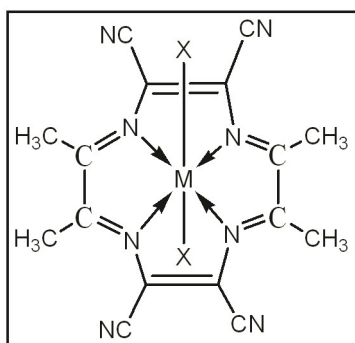


Fig. 4 — Electronic spectrum of $[\text{Co}(\text{C}_{16}\text{H}_{12}\text{N}_{10})\text{Cl}_2]$.



Where $M = \text{Co(II)}, \text{Ni(II)}, \text{Cu(II)}, \text{Zn(II)}$

Fig. 5 — ESR spectrum of $[\text{Cu}(\text{C}_{16}\text{H}_{12}\text{N}_{10})\text{Cl}_2]$.

antifungal activities of the compounds have been evaluated by size of the diameter in mm and by percentage growth of inhibition respectively.

The result of analyzed compounds showed that they were found to hinder the growth of the bacteria and fungi to a considerable extent. The effectiveness of antibacterial and antifungal properties of Schiff base metal complexes were due to presence of cyanide and azomethine groups. Schiff base complexes behave as potent bacteriostatic agents, due to chelation in metal complexes. The reported metal complexes show good antibacterial, antifungal activities and inhibit the microbial, fungal growth. The complexes limit the growth of bacteria by interfering with bacterial protein production, DNA replication bacterial cellular metabolism. The synthesized complexes block respiration process of cell^{26,27}, which leads to limit the proteins synthesis. Inconsistent activity of metal complexes against different microbes depends on impermeability of cells of the microbes.

The complexes may involve in formation of hydrogen bond through azomethine group with the active centers of the cell, resulting in interference with

the normal biological cell process. The antimicrobial activities were not only influenced due to chelation but also due to nature of the ligands, concentration and presence of co ligands, lipophilicity and hydrophilic properties which showed that metal chelates extensively increases antimicrobial activities of complexes. In current study, complexes (2, 3 and 5) have showed the lowest MIC ($7\mu\text{g}/\text{mL}$) against *B. subtilis*, *S. aureus*, *E. Coli*. Complex (5) shows MIC ($9\mu\text{g}/\text{mL}$) against *B. subtilis*. Complexes (2, 3) were most potent against gram positive and negative bacteria as in Table 3. Some of the metal complexes are more effective on gram positive bacteria as compared to the gram negative bacteria. Chemically synthesized complexes were analyzed and compared with commercial available antibiotic (*Ciprofloxacin*). MIC of complex (4) was found to be $6.25\mu\text{g}/\text{mL}$ and complexes (1, 3, 5) showed MIC value of $12.25\mu\text{g}/\text{mL}$ against fungi *Candida albicans*. When compared MIC values of these complexes with MIC of standard antibiotic, it was found that complex 4 was more effective against the fungi *Candida albicans*.

Conclusion

In present study, macrocyclic transition metal complexes of Co^{II} , Ni^{II} , Cu^{II} and Zn^{II} have been prepared from condensation of diaminomaleonitrile and diacetyl in presence of divalent metal ions. Co^{II} , Ni^{II} , Cu^{II} and Zn^{II} complexes have been synthesized and characterized on the basis of analytical, magnetic and spectral data. The Schiff base of macrocyclic complex coordinated through its azomethine nitrogen to the metal ion and acts as neutral tetradentate ligands. All the complexes exhibit distorted octahedral geometry and exhibits potent antimicrobial in comparison to standard antibiotic. Some complexes exhibit more efficient antibiotic properties than standard antibiotic to inhibit the growth of microbes and fungi colonies (Fig. 5).

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