Available on line www.jocpr.com

Journal of Chemical and Pharmaceutical Research

ISSN No: 0975-7384
CODEN(USA): JCPRC5

J. Chem. Pharm. Res., 2011, 3(3):196-204

Synthesis, characterisation and biological activities of Mn(II), Co(II) and Ni(II) complexes of hexamethylenetetramine

M.O. Agwara[1*], M.D. Yufanyi[2], J.N. Foba-Tendo[2], M.A. Atamba[1] and Derek Tantoh Ndinteh[3]

[1]*Coordination Chemistry Laboratory, Department of Inorganic Chemistry, Faculty of Science, University of Yaoundé I, P.O. Box 812 Yaoundé, Cameroon*
[2]*Department of Chemistry, Faculty of Science, University of Buea, P.O. Box 63 Buea, Cameroon*
[3]*Department of Chemical Technology, University of Johannesburg, P.O. Box 17011, Doorfontein, South Africa*

ABSTRACT

Mn(II), Co(II) and Ni(II) complexes of hexamethylenetetramine (HMTA) have been synthesized in water and ethanol. All the complexes are hydrogen-bonded, except the cobalt complex $[Co(HMTA)_2(NO_3)_2(H_2O)_2]$ which is polymeric. These complexes have been characterized by elemental analyses, infrared and visible spectroscopy as well as conductivity. The results suggest octahedral coordination in which the central metal ion is bonded to aqua ligands and the HMTA is bonded to the aqua ligands through hydrogen-bonding. Antibacterial activities of the ligand and its complexes show that the ligand is active against 1 out of 10 tested bacteria species; the cobalt complexes $[Co(H_2O)_6](HMTA)_2(NO_3)_2.4H_2O$, and $[Co(HMTA)_2(NO_3)_2(H_2O)_2]$ are the most active, showing activity against all the microorganisms. These cobalt complexes also show greater activity than the reference antibiotic gentamycin against Klebsiella pneumonia.

Keywords: Hexamethylenetetamine; Antimicrobial; Mn(II); Co(II); Ni(II).

INTRODUCTION

The emergence of antibiotic resistant pathogens and the continuing emphasis on health care costs has provoked a renewed interest in the design and development of novel and cost-effective antimicrobial agents with increased biological activity against the resistant strains [1-6]. Strategies currently being explored to tackle this problem include the structural modification of existing antimicrobial drugs to which resistance has developed and the development of entirely new classes of antimicrobial agents that work on different target sites [1,2]. Broad empirical screening of chemical entities for antimicrobial activity represents an alternative strategy for the development of new antimicrobials [2].

It has been shown that coordination of biologically active organic ligands to metal ions increases their biological activity [8-12]. The complex of ruthenium with clotrimazole has been found to be more active than the uncoordinated clotrimazole against *Trypanosoma cruzi* [13]. Cobalt complexes with some organic ligands have been found to show higher antibacterial activity against *Staphylococcus aureus* and *Enterococcus faecalis* [14]. The importance of bismuth compounds added to clarythromycin or metronidazole in order to eradicate *Helicobacter pylori* has been recognised [15]. Heterocyclic compounds do play important roles in regulating biological activities [8, 16, 17].

Hexamethylenetetramine, $C_6H_{12}N_4$, is a heterocyclic tetradentate donor ligand, which has been used medicinally as an antiseptic agent for the treatment of urinary tract infections [18]. In our recent papers, we reported on the synthesis, characterisation and crystal structure determination of a cobalt(II)-hexamethylenetetramine coordination polymer[19] and a three-dimensional network of an H-bonded Ni(II) hexamethylenetetramine complex[20]. Although a good number of metal complexes of hexamethylenetetramine are reported in literature, there are a few reports, to our knowledge, on their biological activities.

Recognising the antimicrobial properties of this ligand, we have chosen to investigate the effect of complexation on its biological activity.

In this paper, we report the synthesis, characterisation, and antimicrobial activities of hexamethylenetetramine complexes of Mn(II), Co(II), Ni(II), and Zn(II).

EXPERIMENTAL SECTION

Materials

Hexamethylenetetramine (HMTA, $C_6H_{12}N_4$), $C_OCl_2.6H_2O$, and $MnCl_2.4H_2O$ were obtained from Prolabo while, $NiCl_2.6H_2O$, $ZnCl_2$, $Co(NO_3)_2.6H_2O$, $Mn(NO_3)_2.4H_2O$ and $Ni(NO_3)_2.6H_2O$ were obtained from Riedel-de Haën. All the chemicals were of reagent grade and were used without further purification. All solvents used were dried and distilled according to standard methods.

Physical Measurements

Elemental analysis for carbon, nitrogen, and hydrogen were carried out at the Midwest Microlab, LLC Indianapolis, USA and Institute de Chimie Moléculaire de Reims CNRS UMR 6229, Groupe de Chimie de Coordination, Faculté des Sciences, Université de Reims Champagne-Ardenne, France; while Mn(II), Co(II), Ni(II) and Zn(II) were estimated by complexometric titrations[21]. The melting point/ decomposition temperatures of the complexes were obtained using the Mel-Temp II Lab Device. Conductivity measurements were carried out in distilled water using the Vernier LabPro Texas Instruments T189 at room temperature.

The infrared spectra of the ligand and complexes were recorded using pressed KBr discs in the range (4000-400 cm^{-1}) on Perkin-Elmer 457 Spectrophotometer. Electronic spectra were recorded on Hitachi U-2000 spectrophotometer.

Synthesis of the Complexes

Generally, the complexes were prepared by reacting the respective metal salts with hexamethylenetetramine using 1:1 or 1:2 mole ratio, i.e. one mole of metal salt : one mole of hexamethylenetetramine or one mole of metal salt : two moles of hexamethylenetetramine.

For example, **$[Ni(H_2O)_6](HMTA)_2Cl_2.4H_2O$** was synthesised by adding dropwise a solution of hexamethylenetetramine (2.8 g; 2.0 mmol) in 15 mL ethanol to a solution of $NiCl_2.6H_2O$ (4.75 g; 2.0 mmol) in 20 mL water while stirring at ambient temperature. The mixture was further stirred for three hours and the resulting solution allowed to stand for five days, during which green crystals were observed to form. These were filtered, washed with ether and dried *in vacuo*. The other complexes were prepared similarly using the respective mole ratios.

Antimicrobial Tests

The antimicrobial tests were carried out in the Applied Microbiology and Molecular Pharmacology Laboratory (LMP) of the University of Yaoundé I, Cameroon.

Ten species of bacteria namely: *Staphylococcus aureus* (Gram-Positive bacteria), *Shigella flexineri, Escherichia coli, Enterobacter cloacae, Salmonella typhi, Klebsiella oxytoca, Citrobacter freundii, Proteus vulgaris, Morganella morganii and Klebsiella pneumonia* (Gram-negative bacteria) were used for this study. All the species were derived from stock cultures obtained from the Medical Bacteriology Laboratory of "Centre Pasteur du Cameroun", Yaoundé, Cameroon. The microbial isolates were maintained on an agar slant at 4^oC in the Laboratory. The strains were sub-cultured on an appropriate fresh agar plate, 24 hours prior to any antibacterial tests.

Sensitivity Tests: Sample ligand, metal salts and complexes were diluted in sterilized distilled water at 100mg/mL. 1mg of each test compound was placed on a sterilized filter paper disc and allowed to dry. Reference antibiotic (RA), Gentamycin was also prepared in the same manner and 10µg placed on a sterilized filter paper disc and dried, prior to testing.

Diffusion Tests: *In vitro* antibacterial activity of the ligand, metal salts and complexes were evaluated using disc-diffusion method. Mueller-Hinton Agar was employed as microbial growth medium. The antibacterial diffusion tests were carried out as described by Berghe and Vlietink [22] using a cell suspension of about 1.5×10^6CFU/mL obtained from the McFarland Turbidity standard N^o 0.5.

Mueller-Hinton (MH) agar was poured (to a height of 5mm) in to sterile 9cm diameter Petri dishes and allowed to solidify. The solid Mueller–Hinton agar were inoculated with bacteria strains using a platinum wire loop which had been previously sterilized by heating it red hot in a flame, cooled and then used for the application. The dishes were allowed to dry for 10 minutes at 37^0C in an incubator. Sterilized forceps were used for the application of the paper discs containing the test compounds on previously inoculated MH agar dishes, with that of the RA placed at the centre. The plates were kept for 30 minutes at ambient temperature to allow for pre-diffusion, and then incubated at 37^0C for 24 hours. Antimicrobial activity was evaluated [22] by measuring the diameter of growth inhibition zone (IZ) in mm around the discs. Three replicas were performed for each sample and mean values of the growth inhibition zone were calculated. Compounds were considered active when the IZ was greater than 6mm.

RESULTS AND DISCUSSION

The physical and analytical data for the complexes are presented in Table 1. All the complexes have sharp melting points ranging from 140-217°C, an indication that they are pure. The complex of nickel, $[Ni(H_2O)_6](HMTA)_2Cl_2.4H_2O$ changes from green to brown and to navy blue and then melts at 217^OC. The cobalt complex $[Co(H_2O)_6](HMTA)_2(NO_3)_2.4H_2O$ changes from light pink to deep blue and finally to violet and then melted. The variation in the colour with

increasing temperature could be due to changes in the crystal structure from an octahedral to a tetrahedral environment, as water molecules are removed [23,24]. The metal complexes are less intense in colour than the respective metal salts from which they were derived. The complexes are crystalline solids that are air stable and non-hygroscopic as opposed to the starting salts. The elemental analytical results for carbon, hydrogen and nitrogen as well as the estimated metal contents are very close to the calculated values (Table 1).

Table 1: Physical and Analytical Data of the Complexes

Complex	Colour	Melting Point (°C)	Yield (%)	Molar Conductance ($\Omega^{-2}cm^2mol^{-1}$)	Elemental Analysis %Found (%Calculated)			
					%M	%C	%H	%N
$[Ni(H_2O)_6](HMTA)_2Cl_2.\ 4H_2O$ **1**	Green	214	75	198	10.15 (9.95)	24.58 (24.42)	7.74 (7.51)	18.87 (19.02)
$[Ni(H_2O)_6](HMTA)_2Cl_2.\ 2H_2O$ **2**	Green	217	78	197	10.23 (10.26)	25.60 (25.19)	7.73 (7.40)	18.96 (19.59)
$[Mn(H_2O)_6](HMTA)_2(NO_3)_2.2H_2O$ **3**	Dirty White	164	65	110	9.07 (9.12)	23.70 (23.88)	6.48 (6.63)	23.10 (23.21)
$[Co(H_2O)_6](HMTA)_2(NO_3)_2.\ 4H_2O$ **4**	Pink	156	68	191	9.10 (9.16)	22.63 (22.40)	6.89 (6.91)	21.22 (21.77)
$[Co(HMTA)_2(NO_3)_2(H_2O)_2]$ **5**	Pink	148	71	11.5	15.58 (15.62)	20.10 (20.10)	4.50 (4.49)	23.10 (23.40)
$[Ni(H_2O)_6](HMTA)_2(NO_3)_2.4H_2O$ **6**	Green	159	71	127	9.27 (9.13)	22.20 (22.20)	6.69 (6.89)	21.96 (21.78)

The molar conductivities of the metal complexes of hexamethylenetetramine in water (Table 1) suggest a 1:2 electrolyte type (three ions) [25] for the complexes **1-4** and **6**, indicating that the counter ions Cl^- and NO_3^- are in the outer coordination sphere. The value of 11.5 $\Omega^{-2}cm^2mol^{-1}$ obtained for the complex **5**, i.e. $[Co(HMTA)_2(NO_3)_2(H_2O)_2]$ is very low, indicating that the NO_3^- ions are coordinated to cobalt.

The relevant IR band frequencies of the ligand and the complexes are presented in Table 2. The very broad band at 3326-3460 cm^{-1} observed in all the complexes has been assigned to $\upsilon_{(O-H)}$. The band at 1238 cm^{-1} which has been assigned to $\upsilon_{(C-N)}$ for the free ligand, is similar to that reported in literature [24,25].

Table 2: Selected IR Absorption Bands (cm^{-1}) of HMTA and its Complexes

Complex	$\upsilon_{(O-H)}$	$\upsilon_{(H2O)}$	$\upsilon_{(C-N)}$	$\upsilon_{(NO3^-)}$	$\rho_{(CH2)}$	$\upsilon_{(M-O)}$
Hexamethylenetetramine			1238s		810s	
$[Ni(H_2O)_6](HMTA)_2Cl_2.\ 4H_2O$ **1**	3379br	1666m 1623w	1240m		808s	725s
$[Mn(H_2O)_5(NO_3)](HMTA)_2(NO_3).2H_2O$ **3**	3400br	1655br 1630w	1235s	1378s	808w	680s
$[Co(H_2O)_6](HMTA)_2(NO_3)_2.\ 4H_2O$ **4**	3460br	1666m 1625w	1235s	1350s	808s	723m
$[Co(HMTA)_2(NO_3)_2(H_2O)_2]$ **5**	3410br	1630br	1245s 1225w	1378s	821s	732w
$[Ni(H_2O)_6](HMTA)_2(NO_3)_2.4H_2O$ **6**	3326br	1660m 1630br	1238m	1384s	810s	687s

vbr: very broad; br: broad; m: medium; s: strong; w: weak

The strong and sharp band observed at 1763 cm^{-1} for complex **5** shows a monodentate nitrate ion, Co-NO_3^- [19]. This band is split into 1245 cm^{-1} and 1225 cm^{-1} in complex **5**, suggesting that

HMTA is coordinated to the cobalt ion [19,28]. It is not split in the complexes **1-4** and **6**, indicating that HMTA is not coordinated to the metal ion.

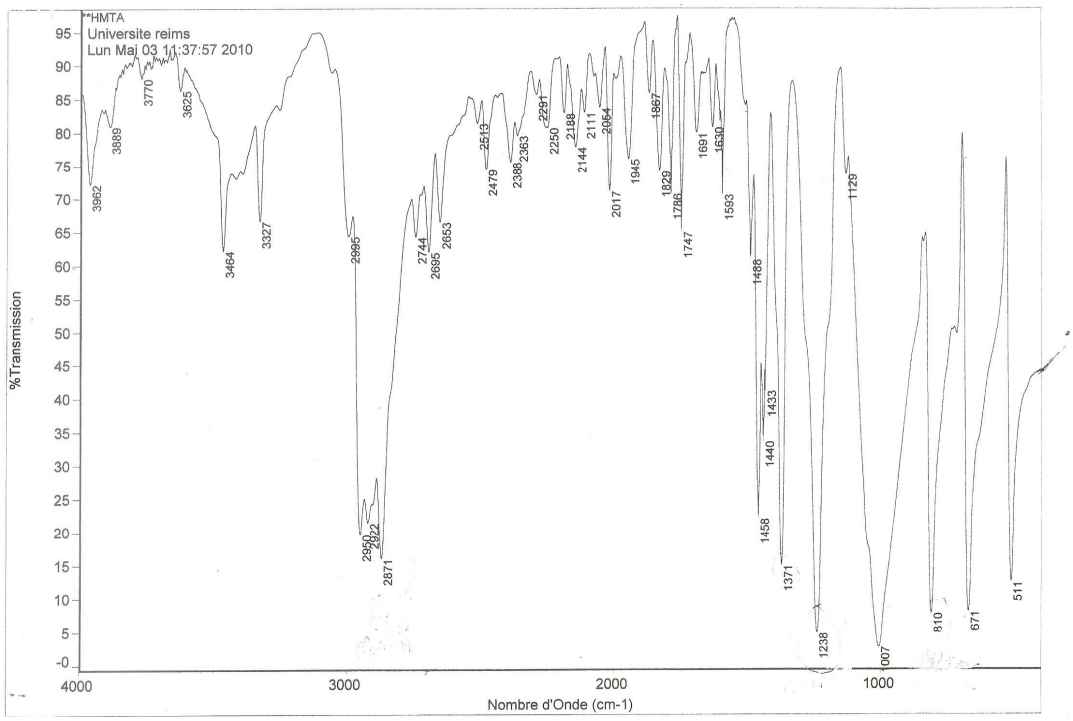

Figure 1: IR Spectrum of Hexamethylenetetramine.

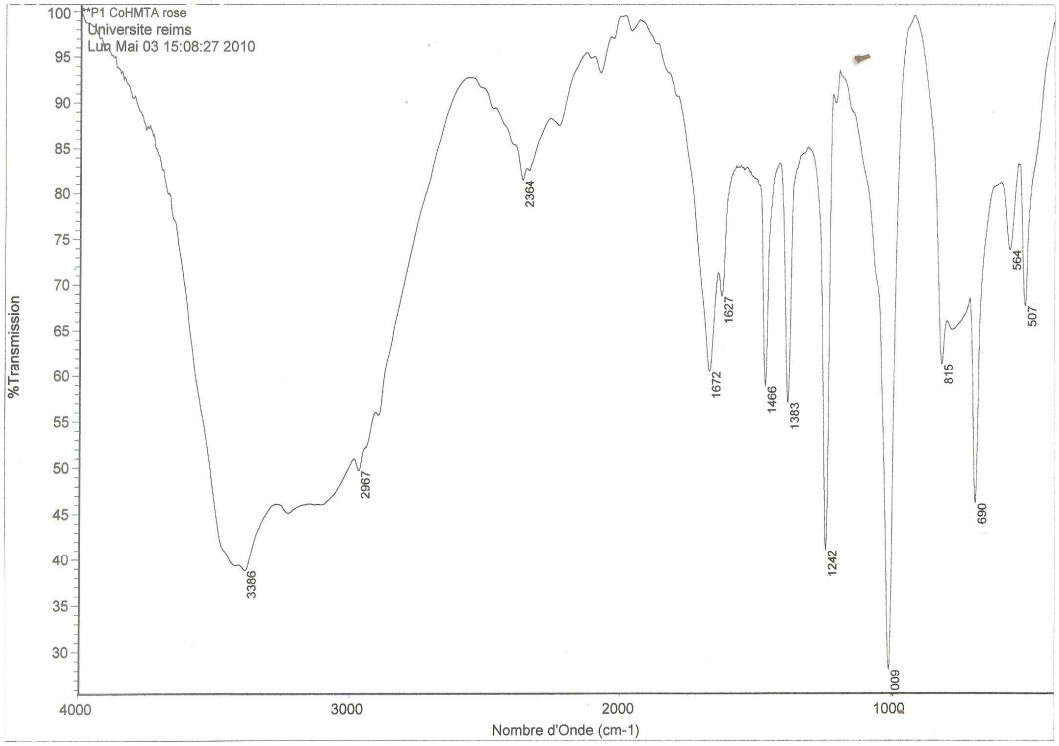

Figure 2. IR Spectrum of Co $(HMTA)_2$ Cl_2 $10H_2O$

The band observed at 810 cm^{-1} in uncoordinated hexamethylenetetramine is similar to those in compounds **1-4** and **6** but in compound **5** it is shifted to 821 cm^{-1} still indicating that HMTA is coordinated to the metal ion in compound **5**. The coordination of water molecules to the cations results in the appearance of a vibrational band at 680-732 cm^{-1} and assigned to $\upsilon_{M\text{-}H2O}$ [10]. A single band for complex **5** at 1630 cm^{-1} indicates that all the water molecules are crystallographically equivalent [29]. Complexes **1-4** and **6** show two bands each at 1660-1666 and 1623-1630 cm^{-1}assigned to ν_{H2O}. This is an indication that there are two types of crystallographically non-equivalent water molecules (coordinated and non-coordinated water molecules) in the complexes [19,29]. Hexamethylenetetramine is most probably bonded to the water molecules and the anions by hydrogen bonds [29,30].

The visible absorption spectral data for some of the complexes are presented in Table 3. The electronic absorption spectra of the cobalt(II) complexes reveals two bands at (21,142, 21,053) cm^{-1} and (19,627, 19,455) cm^{-1}. These two bands have been assigned to

$^4T_{1g}(F) \longrightarrow {}^4T_{1g}(P)$ and $^4T_{1g}(F) \longrightarrow {}^4A_{2g}$ transitions, respectively. Similar bands at 21,500cm^{-1} and 19,000cm^{-1} for Co(II) complexes have been reported in literature [19,20,31] for which octahedral geometry was proposed.

Solution spectra for the nickel(II) complexes reveals a band at (25,126, 24,938) cm^{-1} and a second broad and split band at (14,903-13,569) cm^{-1} which have been assigned to

$^3A_{2g} \longrightarrow {}^3T_{1g}(P)$ and $^3A_{2g} \longrightarrow {}^3T_{1g}(F)$ transitions, respectively. The splitting of the second band is probably due to spin-orbit coupling which mixes the $^3T_{1g}(F)$ and ^1Eg states because they are very close in energy [20,31]. The ratios of 1.67 and 1.69 of the height of the first to that of the second bands for the Ni(II) complexes, is indicative of an octahedral geometry about the nickel ion [32].

Table 3: Band Positions and Proposed transitions for some of the Complexes

Complexes	Band Position	Assignment
$[Ni(H_2O)_6](HMTA)_2Cl_2.4H_2O$	24,938cm^{-1}	$^3A_{2g} \longrightarrow {}^3T_{1g}(p)$
1	14,903 - 13,569cm^{-1}	$^3A_{2g} \longrightarrow {}^3T_{1g}(F)$
$[Co(HMTA)_2(NO_3)_2(H_2O)_2]$	21,142cm^{-1}	$^4T_{1g}(F) \longrightarrow {}^4T_{2g}$
5	19,455cm^{-1}	$^4T_{1g}(F) \longrightarrow {}^4A_{2g}$
$[Ni(H_2O)_6](HMTA)_2(NO_3)_2.4H_2O$	25,126cm^{-1}	$^3A_{2g} \longrightarrow {}^3T_{1g}(p)$
6	14,881 - 13,699cm^{-1}	$^3A_{2g} \longrightarrow {}^3T_{1g}(F)$

Antibacterial Tests

The ligand, metal salt and the metal complexes were tested for antibacterial activity in vitro against ten bacteria strains. The susceptibility of the bacterial strains towards the compounds, judged by measuring the diameter of the growth inhibition zone, is presented in Table 4.

Table 4: Antimicrobial Activities of the Ligand and Complexes (IZ diameter in mm)

Tested Compounds	A_1	A_2	A_3	A_4	A_5	A_6	A_7	A_8	A_9	A_{10}
HMTA	-	-	-	-	7	-	-	-	-	-
1	8	9	9	8	14	11	10	9	9	11
2	8	8	9	11	11	11	12	-	15	13
4	18	12	19	21	17	22	22	20	20	20
5	16	10	23	20	16	19	19	19	18	20
6	11	16	19	14	10	18	16	15	10	17
RA	24	23	23	24	25	24	12	23	23	24

A_1 = Staphylococcus aureus, A_2 = Enterobacter chloacae, A_3 = Schigella flexineri,
A_4 = Escherichia coli, A_5 = Salmonella typhi, A_6 = Morganella morganii,
A_7 = Klebsiella pneumoniae, A_8 = Citrobacter freundii, A_9 = Klebsiella oxytocae
A_{10} = Proteus vulgaris, IZ = Inhibition Zone, RA = Reference Antibiotic (Gentamycin).

All the metal complexes tested, showed some activity against the different types of Gram-positive and Gram-negative bacteria while the hexamethylenetetramine ligand (HMTA), was found to be active against only on one *(S. typhi)* of the 10 pathogens. This increase in activity on coordination could be explained on the basis of Overton's concept and chelation theory [12,16,33]. According to Overton's concept of cell permeability, the lipid membranes that surround the cell favours the passage of only lipid-soluble material and lipid-solubility is an important factor that controls antimicrobial activity. On coordination, the polarity of the metal ion is reduced due to overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with the ligand's donor atoms so that, there is electron delocalization within the whole chelate ring. This may increase the lipophilic character of the metal complex, enabling it to permeate the lipid membrane of the bacteria and thus killing them more effectively. Also, factors such as solubility, different dipole moments and cell permeability mechanisms may be influenced by the presence of the different anions and this affects the mechanism of permeation through the lipid layer of the organisms killing more of them effectively [34].

The pathogens *S. flexineri, E. coli, M. morganii, K. oxytoca* and *P. vulgaris* were inhibited by all the complexes tested. The compounds **1** and **2** are the least active of the tested compounds, while compound **6** is moderately active. The difference in activity between compounds **1** and **2** and compounds **5** and **6** might be due to the change in counter ion from the chloride ion in compounds **1** and **2** to the nitrate ion in compounds **5** and **6**. This means that the chloride ion reduced the antibacterial activity of the metal complexes. The most active compounds are those of cobalt (**4**, **5**), having higher IZ values for most of the bacterial strains tested. We can therefore arrange the complexes in increasing order of activity as: **2** < **1** < **6** < **5** < **4**. The complexes with nitrate as counter ion (**4**, **5**, **6**) are more active than those with chloride as counter ion (**1** and **2**). The complexes of cobalt(II) showed greater activity than those of nickel(II) towards the tested bacteria. This indicates that the coordinated metal may play a significant role in antimicrobial activity. Compounds **4** and **5** were found to be more active than the reference antibiotic against *K. pneumoniae.* Thus, they can be further explored *in vitro* for the treatment of infectious diseases caused by this microorganism.

CONCLUSION

The metal complexes of Mn(II), Co(II) and Ni(II) with HMTA as ligand have been synthesised and characterised by elemental, IR and visible spectroscopy analyses. In compounds **1-4** and **6** the metal atom is bonded to six aqua ligands while the HMTA molecules and the chloride or nitrate ions are bonded to the coordinated and free water molecules through hydrogen bonding. In compound **5**, the cobalt atom is bonded to two nitrate ions, two water molecules and two

HMTA molecules giving a distorted octahedral geometry about the cobalt atom. Antibacterial studies of these complexes against ten bacteria species showed that there is increased activity of the metal ions upon coordination to the ligand. The complexes with nitrate as counter ion (**4**, **5**, **6**) are more active than those with chloride as counter ion (**1** and **2**). The complexes of cobalt(II) showed greater activity than those of nickel(II) towards the tested bacteria. The activity order of the complexes is **2** < **1** < **6** < **5** < **4**. The higher activities of compounds 4 and 5 than that of the reference antibiotic, gentamycin, against the pathogen *K. Pneumonia*, could be further studied and exploited for the treatment of infections caused by this bacterium.

Acknowledgements
We would like to thank Dr. Aminou Mohamadou of Institute de Chimie Moléculaire de Reims CNRS UMR 6229, Groupe de Chimie de Coordination, Faculté des Sciences, Université de Reims Champagne-Ardenne, France for assisting with some of the analyses and Dr. Bogne Kamga Patrice of the Laboratory of Applied Microbiology and Molecular Pharmacology, University of Yaounde 1, Cameroon, for running the antibacterial tests.

REFERENCES

[1] M. Rai, A. Yadav and A. Gade, *Biotechnology Advances*, **2009**, 27(1), 76-83.
[2] T.P. Tim Cushnie, A. J. Lamb, *International Journal of Antimicrobial Agents*, **2005**, 26, 343–356.
[3] J.S. Kim, E. Kuk, K.N. Yu, J.-H. Kim, S.J. Park, H.J. Lee, S.H. Kim, Y.K. Park, Y.H. Park, C.-Y. Hwang, Y.-K. Kim, Y.-S. Lee, D.H. Jeong, M.-H. Cho, *Nanomedicine: Nanotechnology, Biology, and Medicine*, **2007**, 3, 95– 101
[4] T.E. Cloete, *International Biodeterioration and Biodegradation*, **2003**, 51, 277-282.
[5] R.N. Patel, N. Singh, K.K. Shukla, U.K. Chauhan, J. Niclos -Gutierrez, A. Castineiras, *Inorg. Chim. Acta*., **2004**, 357(9), 2469-2476.
[6] W. Xiaohui, D. Yumin, F. Lihong, L. Hui and H. Ying, *Polymer Bulletin*, **2005**, 55, 105-113.
[7] K. Nomiya, T. Satoshi, R. Noguchi, *J. Chem. Soc., Dalton Trans*. **2000**, 4369- 4373.
[8] L. Jian, L. Tingting, C. Sulan, W. Xin, L. Lei, W. Yongmei, *J. Inorg. Biochem*., **2006**, 100(11), 1888-1896.
[9] Golcu, M. Tumer, H. Demirelli and R.A. Wheatly, *Inorg. Chim. Acta*, **2005**, 358, 1785-1797.
[10] M.O. Agwara, P.T. Ndifon, M.K. Ndikontar, and M.A. Atamba, *Res. J. Chem. Environ.*, **2008**, 12(1), 87-92
[11] M.O. Agwara, P.T. Ndifon, N.B. Ndosiri, A.G. Paboudam, D.M. Yufanyi and A. Mohamadou, *Bull. Chem. Soc. Ethiop*., **2010**, 24(3), 1-7.
[12] P.T. Ndifon, M.O. Agwara, J.N. Njapba, D.M. Yufanyi, A.G. Paboudam and L.D. Nyamen, *Res. J. Chem. Environ*., **2010**, 14(2), 50-54.
[13] R.A. Sanchez-Delgado, K. Lazardi, L. Rincon, J.A. Urbina, A.J. Hubert and A.N. Noels, *J. Med. Chem.*, **1993**, 36, 2041-2043.
[14] R.A. Sheikh, S. Shreaz, L.A. Khan, A.A. Hashmi, *J. Chem. Pharm. Res.,* **2010**, 2(3), 274-286
[15] F. Novelli, M. Recine, F. Sparatore, and C. Juliano, *Il Farmaco*, **1999**, 54, 232–236.
[16] R. Shakru, N. J. P. Subhashini, Sathish Kumar K., Shivaraj, *J. Chem. Pharm. Res.,* **2010**, 2(1), 38-46
[17] K.S. Abou-Melha and H. Faruk, *Iran. Chem. Soc.,* **2008,** 5(I), 122-134
[18] S. Miall, L. Mackenzie, A Dictionary of Chemistry, Longmans, London, **1956**, 252.
[19] P.T. Ndifon, M.O. Agwara, A.G. Paboudam, D.M. Yufanyi, J. Ngoune, A. Galindo, E. Alvarez, A. Mohamadou, *Transition Met. Chem*., **2009**, 34, 745-750.

[20] M.O. Agwara, P.T. Ndifon, M.D. Yufanyi, J.N. Foba Tendo, M.A. Atamba, A.G. Paboudam, A. Galindo, E. Alvarez, *Rasayan J. Chem.*, **2010**, 3(2), 207-213.
[21] D.C. Harris, Quantitative Chemical Analysis, W.H. Freemans, New-York, **1991**, 279-299.
[22] A.V. Berghe and A.J. Vlietink, *Methods for Biochemistry*, **1991**, 6, 47-68.
[23] K. Nagase, H. Yokobayashi, K. Sone, *Bulletin of the Chemical Society of Japan*, **1976**, 49(6), 1563-1567.
[24] K.S. Patel and M.O. Agwara, *Nig. J. Science,* **1990,** 24(1&2), 104-108.
[25] W.J. Geary, *Coordination Chemical Review*, **1971**, 7, 81-82.
[26] A.A. Ennan, L.A. Gavrilova, T.S. Borisenko, *Russ. J. Inorg. Chem*., **1976**, 21(4), 536-538.
[27] A.W. Baker, *J. Phys. Chem*., **1957**, 61, 450.
[28] J.O. Jensen, *Spectrochimica Acta Part A,* **2002**, 58, 1347-1364.
[29] T.G. Balicheva, I.V. Pologikh, *Russ. J. Inorg. Chem*., **1975**, 20(12), 1769-1773.
[30] T.G. Balicheva, I.V. Pologikh, D.I. Kovachev, A.J. Statelova, *Russ. J. Inorg. Chem*., **1975**, 20, 87 – 90.
[31] M.O. Agwara, P. T. Ndifor, M. K. Ndikontar, *Bull. Chem.Soc, Ethiop.* **2004,** 18(2), 143-148.
[32] D.L. Sutton, Electronic Spectra of Transition Metal Complexes, McGraw-Hill, London, **1968**, 129.
[33] Z.H. Chohan, M.K. Khahid, T.S. Claudiu, *Appl. Organomet. Chem.,* **2004,** 18, 305-310.
[34] Z.H. Chohan, A. Rauf, C.T. Supuran, *Metal Based Drugs*, **2002**, 8(5), 287-291.