Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2016, 8(12):144-151

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis, Characterization and Antimicrobial Properties of Some Co (II) Complexes of Hexamethylenetetramine

Che Dieudonne Tabong[1], Divine Mbom Yufanyi[2], Donatus Bekindaka Eni[1] and Moise Ondoh Agwara[1*]

[1]Department of Inorganic Chemistry, Faculty of Science, University of Yaoundé I, Yaoundé, Cameroon
[2]Department of Chemistry, Faculty of Science, The University of Bamenda, Bamenda, Cameroon

---

ABSTRACT

Four Co(II) complexes of hexamethylenetetramine (HMTA), $[Co(HMTA)_2(NO_3)_2(H_2O)_2]$, $[Co(HMTA)(SCN)_2(H_2O)_3]$, $[Co_2(HMTA)(N_3)_3(H_2O)_5]$ and $[Co(HMTA)(DCA)_2(H_2O)]$. H_2O have been synthesized and were characterized by physico-chemical and spectroscopic methods. The results suggest that these complexes are octahedral, stable in air and non-hygroscopic as opposed to the starting metal salt. The ligands, metal salt and the complexes were also evaluated for their antimicrobial activities in vitro against seven pathogens.

Keywords: Cobalt (II); Hexamethylenetetramine; thiocyanate; azide; dicyanamide; Antimicrobial

---

INTRODUCTION

Transition metal complexes of N-donor ligands are of interest due to their applications in biology, pharmacology, magnetism, etc. Among these ligands is hexamethylenetetramine (HMTA), a potential tetradentate ligand or hydrogen bond acceptor suitable in self-assembly systems. HMTA is a commercially available organic molecule which possesses three fused rings in the chair conformation similar to the cage-like structure of adamantine [1]. It is a cheap, eco-friendly and readily available for reactions with many hydrated salts. It forms molecular complexes, with varied coordination patterns ranging from monodentate [2], bridging [3, 4], non-chelating to hydrogen-bonded frameworks [5-7], inducing the formation of one-, two- and three-dimensional framework structures. Biologically, HMTA has found applications as a cosmetic biocide in eye make-up preparation, preservative in lotions and creams and antiseptic agent for the treatment of urinary tract infections [8, 9]. Recently, interest in HMTA has increased due to the enhanced thermodynamic and kinetic stability of its metal complexes, and their application in various activities such as anticancer, antitubercular, antibiotic, antimicrobial and antifungal agent [10, 11].

Cobalt is an essential metal element widely distributed in the biological systems. It is a component of vitamin B_{12} complex that is useful in the prevention of anaemia and the production of erythrocytes. Interest in cobalt complexes has also increased due to their therapeutic and biological applications [12].

Among the inorganic anions serving as co-ligands, thiocyanate SCN^- (an ambidentate ligand) is very important due to its great tendency to combine with a variety of metal ions, forming either thiocyanato (M-SCN) or isothiocyanato (M-NCS) complexes and also bridges metal ions. The nature of these complexes depends on the inter-play between the metal ion, the counter ion and HMTA [13].

The nitrate anion can function as a bidentate, bridging or monodentate ligand or as an ionic species in different complexes. The bonding type is probably a function of the nature and number of other ligands present.[14, 15]

The azide anion, N_3^-, is a versatile ligand which can bind to metal ions in several coordination modes: terminal mode via one nitrogen donor, as a bridge ($\mu_{1,1}$) via one nitrogen donor, and in the $\mu_{1,3}$ way via both of the peripheral nitrogen donor atoms.[16] The azide anion coordinated to transition metals has been intensively studied for diverse applications.[17, 18]

In order to fight against antimicrobial resistance, our research team has recently focused on the synthesis and antimicrobial screening of some transition metal complexes of the ligands hexamethylenetetramine [19], pyridine [20], pyridine-2-carboxylic acid [21], 2-aminopyridine [22] and 1,10-phenanthroline.[23, 24] The upsurge of resistant pathogens impedes the effective prevention and treatment of an ever-increasing variety of infections caused by bacteria, parasites, viruses and fungi [25]. This increasing resistance of microbes to antibacterial and antifungal drugs has necessitated the search for new compounds to target pathogenic microbes [25, 26]. Several efforts have been made to develop antimicrobial agents to fight against these resistant pathogens amongst which are the protection of the efficacy and appropriate use of existing drugs as well as research and development of new antimicrobial agents that are not affected by the currently known, predicted, or unknown mechanisms of resistance [27-29]. The incorporation of metals into antibacterial molecules is expected to enhance the bactericidal or fungicidal properties of these drugs.

In view of the varied applications of cobalt complexes and exploring the good biological properties of cobalt and HMTA as well as the structure-directing properties of SCN^-, NO_3^- and N_3^-, we report herein the synthesis and structure elucidation of cobalt(II) complexes of HMTA, SCN^-, N_3^- and NO_3^-. The effects of the co-ligands on the biological activities of the complexes towards some resistant pathogens, evaluated using in vitro assays, are also presented.

EXPERIMENTAL

Materials

$Co(NO_3)_2{\cdot}6H_2O$, hexamethylenetetramine, ammonium thiocyanate and sodium azide were obtained from Sigma Aldrich. The chemicals were of analytical grade and were used without further purification. Methanol was obtained from Reidel-De Haen (Germany). All solvents used were distilled according to standard methods.

Methods

Generally, the complexes were prepared by the reaction of the metal salt, $Co(NO_3)_2.6H_2O$ with the ligands at room temperature.

Synthesis of $[Co(HMTA)_2(NO_3)_2(H_2O)_2]$

$Co(NO_3)_2{\cdot}6H_2O$ (0.528 g; 1 mmol) in 20 mL methanol was added drop wise into a solution of HMTA (0.28 g; 2 mmol) in 20 mL methanol while stirring. The mixture was then stirred for 4 hours and the pink precipitate formed was filtered, washed with diethylether and dried in vacuum over silica gel. Light pink crystals were obtained from the filtrate, at room temperature, after three weeks.

Synthesis of $[Co(HMTA)(SCN)_2(H_2O)_3]$

$Co(NO_3)_2{\cdot}6H_2O$ (0.291 g; 1 mmol) in 15 mL methanol was added drop wise into a solution of HMTA (0.560 g; 2 mmol) in 15 mL methanol while stirring. The solution was stirred for 1 hour at room temperature. Ammonium thiocyanate (0.156 g; 2 mmol) in 10 ml methanol was added into the solution and the mixture was further stirred for 3 hours. The precipitate formed was filtered, washed with diethylether and dried in vacuum over silica. Light pink crystals were obtained from the filtrate, at room temperature, after two weeks.

Synthesis of $[Co(HMTA)(DCA)_2(H_2O){\cdot}H_2O]$

$Co(NO_3)_2{\cdot}6H_2O$ (0.291 g; 1 mmol) in 15 mL methanol was added drop wise into a solution of HMTA (0.560 g; 2 mmol) in 15 mL methanol while stirring. The solution was stirred for 1 hour at room temperature. Sodium dicyanamide (0.36 g; 2 mmol) in 10 ml methanol was added into the solution and the mixture was further stirred for 3 hours. The precipitate formed was filtered, washed with diethylether and dried in vacuum over silica. Purple crystals were obtained from the filtrate, at room temperature, three weeks.

Synthesis of $[Co_2(HMTA)(N_3)_3(H_2O)_5]$

$Co(NO_3)_2{\cdot}6H_2O$ (0.291 g; 1 mmol) in 15 mL methanol was added into a solution of HMTA (0.560 g; 2 mmol) in 15 mL methanol while stirring and the solution was stirred for 1 hour at room temperature. Sodium azide (0.260 g; 2 mmol) in 10 ml H_2O/methanol (1:5 v/v) was added into the solution. The mixture was further stirred for 3 hours and the precipitate formed was filtered, washed with diethylether and dried in vacuum over silica gel. Light pink crystals were obtained from the filtrate, at room temperature, after two weeks.

Characterization

Microanalyses for carbon, hydrogen and nitrogen in the compounds were carried out on a Flash 2000 Thermo Scientific analyser. The infrared spectra was recorded on a Bruker ALPHA-P spectrophotometer directly on a small sample of the complex in the range of 400 - 4000 cm^{-1}, while the UV-visible spectrum of an aqueous solution of the complex was recorded using a Bruker HACH DR3900 UV-Visible spectrophotometer at room

temperature. Melting point/decomposition temperatures of the complexes were obtained using a STUART Scientific Melting Point SMP1 device with maximum temperature at 360^{o}C. Conductivity of the complexes was measured in distilled water using the HACH HQ14d Instrument at room temperature.

Antimicrobial Tests

The *in vitro* antimicrobial tests were carried out in the Laboratory of Phytobiochemical and Medicinal Plant Study, University of Yaoundé I, Cameroon. Four strains of bacteria (*Salmonella enterica*, *Shigella flexineri*, *Escherichia coli* and *Staphylococcus aureus*) and three strains of fungi (*Candida albicans*, *Candida parapsilosis* and *Candida krusei*) were used for this study. All the species were derived from stock cultures obtained from the Medical Bacteriology Laboratory of Centre Pasteur Yaoundé, Cameroon. Reference antibacterial drug chloramphenicol and reference antifungal drug fluconazole were evaluated for their antibacterial and antifungal activities and their results were compared to those of the free ligands and the complex. The disc diffusion method, using Muller Hinton Agar, from the protocol described by the National Committee for Clinical Laboratory Standard (NCCLS, 2004) was used for preliminary screening.

Mueller-Hinton agar was prepared from a commercially available dehydrated base according to the manufacturer's instructions. Several colonies of each microorganism was collected and suspended in saline (0.9% NaCl). Then, the turbidity of the test suspension was standardized to match that of a 0.5 McFarland standard (corresponds to approximately 1.5 x 10^8 CFU/mL for bacteria or 1 x 10^6 to 5 x 10^6 cells/mL for yeast). Each compound or reference was accurately weighed and dissolved in the appropriate diluents (DMSO at 10%, Methanol at 10% or distilled water) to yield the required concentration (2 mg/mL for compound or 1 mg/mL for reference drug), using sterile glassware. Whatman filter paper No. 1 was used to prepare discs approximately 6 mm in diameter, which were packed up with aluminum paper and sterilized by autoclaving. Then, 25 µL of stock solutions of compound or positive control were delivered to each disc, leading to 50 µg of compound or 25 µg of reference drug.

The dried surface of a Müeller-Hinton agar plate was inoculated by flooding over the entire sterile agar surface with 500 µL of inoculum suspensions. The lid was left ajar for 3 to 5 minutes to allow for any excess surface moisture to be absorbed before applying the drug impregnated discs. Discs containing the compounds or antimicrobial agents were applied within 15 minutes of inoculating the MHA plate. Six discs per petri dish were plated. The plates were inverted and placed in an incubator set to 35°C. After 24 hours (for bacteria) and 48 hours (for yeasts) of incubation, each plate was examined. The disc diameter and the diameter of the zones of complete inhibition (as judged by the unaided eye) were measured. Zones were measured to the nearest whole millimetre, using sliding callipers, which was held on the back of the inverted petri plate. Three replicas were performed for each sample and mean values of the growth inhibition zone (IZ) were calculated. Compounds were considered active when the IZ was greater than 6 mm.

Minimum Inhibitory Concentration

The microbroth dilution method was used to determine the minimum inhibitory concentration (MIC) of the compounds and the reference antibiotic on a given microorganism. A polystyrene tray containing 80 wells is filled with small volumes of serial two-fold dilutions of the complex and reference antibiotics. The inoculum suspension and standardization is done according to McFarland standard. The bacterial inoculum is then inoculated into the wells and incubated at 37°C overnight while the fungi is incubated for 48 hours. The lowest concentration of antibiotic that completely inhibits visual growth of bacteria (no turbidity) is recorded as MIC.

The MBC and MFC were determined by transferring 25 µL aliquots of the clear wells into 100 µL of freshly prepared Muller Hinton Broth medium and incubating at 35 °C for 24 hour. MBC is the lowest concentration of test sample which did not produce turbidity as above, indicating no microbial growth. All tests were performed in triplicates.

RESULTS AND DISCUSSION

Synthesis of the complexes

The reaction of $Co(NO_3)_2.6H_2O$ and HMTA with thiocyanate, nitrate, azide or dicyanamide in methanol yielded four complexes whose physicochemical properties are summarised in Table 1. The complexes which are coloured and air stable were obtained in good yields (>65 %). Complexes 1 and 2 had sharp melting points (148ºC and 174°C, respectively) indicating their purity while the complex 3 decomposes at 210°C. Complexes 1 and 2 underwent colour changes at 85°C to brown and 95°C to purple, respectively. Complex 3 changed color from purple to brown at 224°C but remained stable up to 360°C (maximum limit of device). Complex 4 also changed color from light pink to brown at 195°C and decomposed at 224°C. The molar conductivity values of the complexes in water were in the range 16 to 41 $\Omega cm^{-2}mol^{-1}$ indicating that the complexes are non-electrolytes and are molecular.

Table 1: Physical and Analytical Data of the Complexes

Complexes	Colour	Melting Point/oC	Conductivity (Ωcm-2mol-1)	%yield	Elemental Analyses % Found (% Calc.)			
					%C	%H	%N	%Co
Co(HMTA)2(NO3)2(H2O)2 (1)	Pink	148	37.5	72	28.73	5.82	27.56	11.63
					-28.86	-5.65	-28.05	-11.8
Co(HMTA)(SCN)2(H2O)3 (2)	Pink	174	27.3	65	24.9	5.1	21.73	15.42
					-25.7	-4.85	-22.47	-15.21
[Co2(HMTA)(N3)3(H2O)5] (3)	Purple	210 (decompose)	41.5	81	15.19	4.18	39.83	24.12
					-15.2	-4.68	-38.4	-24.22
[Co(HMTA)(DCA)2(H2O)].H2O (4)	Light pink	>360	16.6	94	32.62	4.21	38.18	15.95
					-32.71	-4.39	-38.14	-16.05

Infrared Spectroscopy

The relevant vibrational frequencies of hexamethylenetetramine and the complexes are presented in Table 2.The broad hypsochromic bands at 3435-3390 cm^{-1} observed in all the complexes has been assigned to the υ_s(O-H) vibration. In the complexes, the signals of υ_s(O-H) are blue shifted to 3500-3700 cm^{-1}, become sharper and can be differentiated due to the effect of oxygen donation to the Co^{2+} which weakens the O-H bonds. The υ_s and υ_{as} vibrations of the methylene groups of HMTA appear between 3003 and 2887 cm^{-1}. These symmetric and asymmetric stretching bands overlap with the ν_s(O-H) in complex 2. In the IR spectra of complexes 2, 3 and 4 very strong, characteristic peaks originating from the azide N=N [24, 30], thiocyanate [31] and dicyanamide C=N bond [32] stretching vibrations were observed at 2107 cm^{-1}, 2130 cm^{-1} and 2207 cm^{-1}, respectively. Also, in complex 2, weak symmetric vibrations were observed at 787 cm^{-1} corresponding to C-S stretching vibrations of thiocyanate.

The coordination of water molecules to the cobalt ion results in the appearance of a vibrational band at 697-702 cm^{-1} and assigned to υ[(M-H_2O)] [20, 33]. A single band for the complex 1, 2 and 3 at 1675 cm^{-1}, 1664 cm^{-1} and 1625 cm^{-1}, respectively indicates that all the water molecules are crystallographically equivalent [34, 35]. The spectrum of complex 4 showed two bands at 1673 and 1606 cm^{-1} assigned to νH_2O. This is an indication that there are two types of crystallographically non-equivalent water molecules (coordinated and non-coordinated water molecules) [35-38].

Table 2: Relevant IR (cm^{-1}) bands of HMTA and the metal complexes

HMTA	1	2	3	4	Assignment
-	3501br	3390vbr	3414br	3435br	ν(OH) (coordinated water)
-				3248	ν(OH) (lattice water)
2955		3002s	3003m	2971s	ν(CH_2)
		2971s	2966w,	2887w	
-		, 2073vs,	-	-	CN (of SCN)
		-	2130vs	-	CN of DCA
-		-	-	2207vs	N=N=N stretching
-	1780		1738w		Co-NO_3
-	1675	1664	1625w	1673	HOH bend (*ν*M-H_2O)
				1606	HOH bend (lattice water)
1457	1475	1465	1458	**1462**	ν(CH_2) scissor (HMTA)
1370	1349	1382	1362	1366	ν(CH_2) wag (HMTA)
			1301		*ν*N-O (nitro)
1236	1240	1252	1238	1240	ν(CH_2) rock (HMTA)
	1227	1201	1224		
1000	1002	1031vs	1014	1027	ν(CN) stretch (HMTA)
812	819	827	802	808	ν(CN) stretch (HMTA)
		787	774	778	
		755			C-S of SCN
6,70,690	682	697	700s	,705s	H_2O
		6,73,655	660	678	N-C-N bend (HMTA)
			624		N=N=N
	504	515	516s	526	M-O stretch
		478,	495w, 458	475w	M-N stretch*

The band at 1236cm^{-1}, assigned to the $\nu(CH_2)$ rocking vibration of the free HMTA ligand is observed at 1238-1252cm^{-1} in all the complexes. This band is observed at 1240 cm^{-1} in complex **4** and split into 1240 and 1227 cm^{-1}; 1252 and 1201 cm^{-1} ; and 1238 and 1224 cm^{-1} in complexes **1**, **2** and **3**, respectively, suggesting that HMTA is coordinated to the cobalt ion [34, 39]. The C-N stretching vibration of HMTA which normally appears at 1000 cm^{-1} in the free ligand are red shifted to 1002-1031 cm^{-1} in all the complexes while the C-N peak at 812 cm^{-1} is blue shifted to 802 and 808 cm^{-1} in **3** and **4** while it is red shifted to 819 and 827 cm^{-1} in **1** and **2**, respectively.

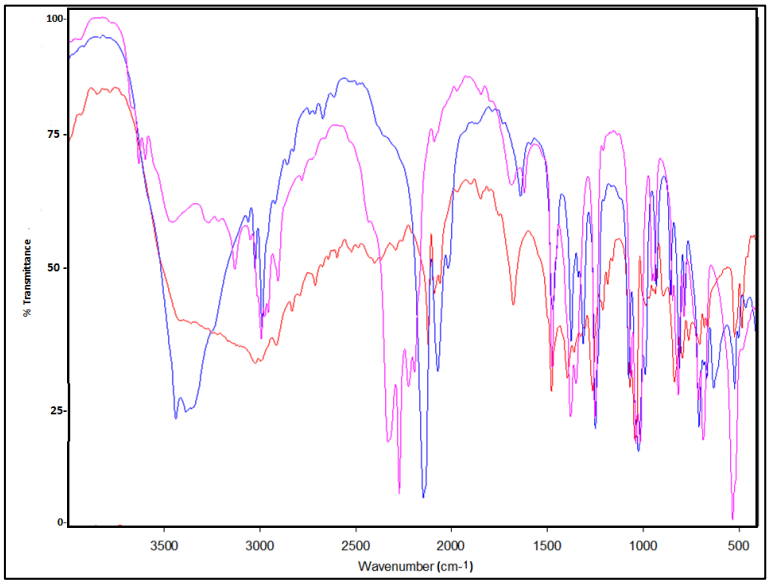

Figure 1: IR Spectra complexes 1 (orange), 2 (red), 3 (blue) and 4 (pink)

UV–Vis Spectroscopy

The electronic spectral data of the complexes in water are presented in Table 3. The electronic absorption spectra reveal two bands each for the complexes (1 – 4). These bands have been assigned to $^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ and $^4T_{1g}(F) \rightarrow {}^4A_{2g}$ transitions respectively. Similar bands have been reported in literature suggesting an octahedral geometry around the cobalt(II) ion [38].

Table 3: Electronic Spectral data of the complexes

Complex	ν_{max} (cm^{-1})	Band Assignement
1	20,790	$^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$
	19,608	$^4T_{1g}(F) \rightarrow {}^4A_{2g}$
2	20,833	$^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$
	19,646	$^4T_{1g}(F) \rightarrow {}^4A_{2g}$
3	19,231	$^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$
	19,157	$^4T_{1g}(F) \rightarrow {}^4A_{2g}$
4	21,322	$^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$
	19,685	$^4T_{1g}(F) \rightarrow {}^4A_{2g}$

Antimicrobial Tests

The metal salt, ligands, metal complexes and the reference antibiotic and reference antifungal drugs were tested for antimicrobial activity in vitro against four bacteria and three fungi strains. The susceptibility of the bacteria and fungi strains towards the compounds was judged by measuring the diameter of the growth inhibition zone. The results are summarized in Table 4 and presented in Figure 2.

Table 4: Inhibition Zone (diameter in mm) of compounds against bacteria and fungi

Compounds	Bacteria				Fungi		
	A_1	A_2	A_3	A_4	B_1	B_2	B_3
NH_4SCN	6±0.0	6±0.0	0	6±0.0	0	6±0.0	0
NaN_3	0	7±0.0	17±1.4	9.5±0.7	0	6±0.0	0
DCA	6	6	6	9	7.5	8	6
HMTA	0	0	0	9±1.4	0	8.5±0.7	30±0.0
$Co(NO_3)_2.6H_2O$	9.5±0.7	0	6±0.0	6.5±0.7	0	6±0.0	0
1	8±0.0	7±0.0	6±0.0	10±0.0	0	6±0.0	0
2	8.5±0.7	9±0.0	7.5±0.7	11.5±0.7	10.5±0.7	7.5±0.7	6.5±0.7
3	10±0.0	12.5±0.7	6±0.0	15.5±0.7	0	6±0.0	0
4	9±1.4	10±1.4	18±0.0	10±0.0	12±1.4	8.5±0.7	11.5±0.7
RA	22±0.0	20±0.0	19±1.4	20±0.0	/	/	/
RB	/	/	/	/	30±0.0	32±0.0	22±0.0

A_1= *Staphylococcus aureus*, A_2 = *Salmonella enterica*, A_3 = *Shigella flexineri*, A_4 = *Escherichia coli*, B_1 = *Candida albicans*, B_2=*Candida parapsilosis*, B_3=*Candida krusei*, RA=Reference Antibacterial (Chloramphenicol), RB = Reference Antifungal (Fluconazole), / = not tested

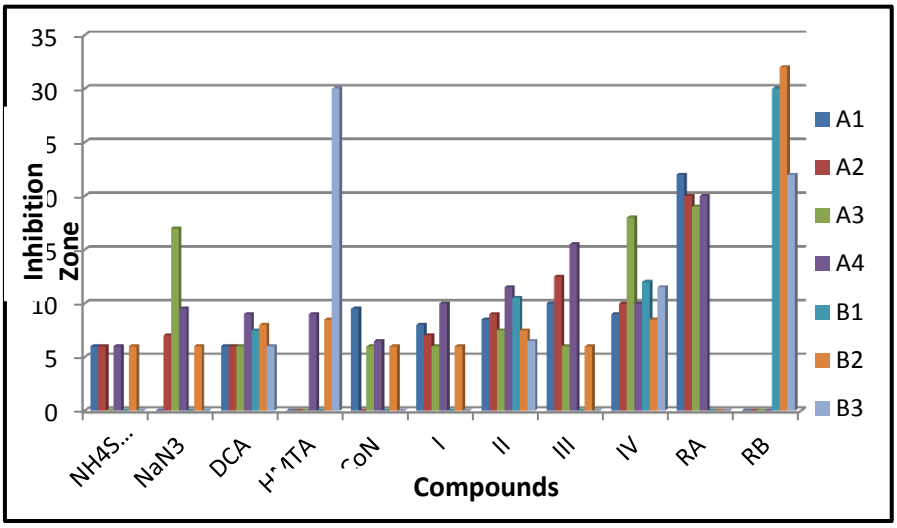

Figure 2: Inhibition zone of ligands, metal salt and complexes against microorganisms

The active compounds **1**, **2**, **3** and **4** were further evaluated in order to confirm their activity by measuring their Minimal Inhibitory Concentrations (MIC). The results are presented in Table 5.

Table 5: Minimal Inhibitory Concentrations (mg/ml) of the complexes 1, 2, 3 and 4

Complexes	Bacteria				Fungi		
	A_1	A_2	A_3	A_4	B_1	B_2	B_3
1	0.62±0.00	1.25±0.00	0.62±0.00	1.25±0.00	0.62±0.00	0.62±0.00	1.25±0.00
2	1.25±0.00	1.25±0.00	1.25±0.00	1.25±0.00	0.62±0.00	0.625±0.00	0.31±0.00
3	0.62±0.00	0.62±0.00	0.62±0.00	1.25±0.00	0.31±0.00	0.31±0.00	0.31±0.00
4	0.62±0.00	0.62±0.00	0.62±0.00	1.25±0.00	0.31±0.00	0.62±0.00	0.62±0.00
RA	0.078±0.00	0.019±0.00	0.008±0.00	0.014±0.007	/	/	/
RB	/	/	/	/	0.016±0.00	0.032±0.00	0.032±0.00

The ligand (HMTA) was found to be active only on one *(Escherichia coli)* of the bacteria strains. Dicyanoamide (DCA) showed mild activity against all the bacteria. The ligands NH_4SCN and NaN_3, each showed low activity against three of the bacteria strains and no activity against *Shigella flexineri and Staphylococcus aureus*,

respectively. All the metal complexes tested, showed some activity against bacteria. This increase in activity on coordination could be explained on the basis of Overton's concept and chelation theory [40-42]. According to Overton's concept of cell permeability, the lipid membranes that surround the cell favors 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 [35, 43].

All the test compounds were active against the fungus *Candida parapsilosis*. The fungi *Candida albicans* and *Candida krusei* were inhibited by complexes **1**, **3** and all the ligands except DCA. Complexes **2** and **4** showed good activity against all the fungi strains. This shows an increase in antifungal activity upon introduction of the thiocyanate and dicyanamide ions into the coordination sphere. The most active complexes are **2** and **4**. The tested compounds are arranged in increasing order of activity as follows: **4** > **2** > **3** > **1** > DCA> $Co(NO_3)_2.6H_2O$ > NaN_3 > NH_4SCN.

CONCLUSION

Four mixed ligand Co(II) complexes with HMTA and nitrate, thiocyanate, azide or dicyanamide co-ligands have been reported. The complexes are octahedral. The results of the preliminary antimicrobial screening against four pathogenic bacteria and three fungi species indicates that complexes **2** and **4** are very active and could be further screened in vitro against a wide range of pathogens. The complexes have activities higher than that of the metal salt and ligands towards the microorganisms. The most sensitive strains are the bacteria species *Escherichia coli* and *Shigella flexineri.* Complexes **2** and **4** showed broad range activity against all the bacteria and fungi strains. Both complexes (**2** and **4**) may represent good candidates as antimicrobial agents. However, additional and profound *in vitro* antimicrobial studies mainly in relation to elucidation of the mechanism of growth inhibition and toxicity of the complexes are necessary.

ACKNOWLEDGEMENT

AMO and DMY acknowledge the Government of Cameroon for financial support through the Fonds d'Appuis à la Recherche. The authors thank the Laboratory of Phytobiochemical and Medicinal Plant Study, University of Yaounde I for the antimicrobial tests.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

REFERENCES

[1] AM Kirillov. *Coord Chem Rev*, **2011**, 255(15–16), 1603-1622.
[2] MK Ammar; T Jouini and A Driss; *Chem Cryst*, **2000**, 30(4265).
[3] A Ray; J Chakraborty; B Samanta; S Thakurta; C Marschner; MS El Fallah; S Mitra. *Inorg Chim Acta*, **2008,** 361(7), 1850-1860.
[4] Y Chen; Y-L Wang; S-M Ying; S-L Cai. *Acta Crystallogr*, **2007**, E63(11), m2751.
[5] A Trzesowska; R Kruszynski. *Trans Met Chem*, **2007**, 32(625 - 633).
[6] X-L Li; Z-S Lu; D-Z Niu. *Acta Crystallogr*, **2007,** E63(11), m2640.
[7] D Pritesh; C Deepak; AS Prakash; R Guru; MS Hegde. *J Cryst Growth*, **2004,** 275(e2043), 1-2.
[8] MO Agwara; DM Yufanyi; JN Foba-Tendo; MA Atamba; DT Ndinteh. *J Chem Pharm Res*, **2011,** 3(3), 196-204.
[9] L S Miall; Mackenzie. *A Dictionary of Chemistry, Longmans*, **1956**.
[10] MO Agwara; PT Ndifon; MK Ndikontar. *Bull. Chem Soc Ethiopia*, **2004,** 18(2), 143-148.
[11] KS Prasad; LS Kumar; HD Revanasiddappa; B Vijay; B Jayalakshmi. *Aston j*, **2011** CSJ-12
[12] A Mishra; NK Kaushik; AK Verma; R Gupta. *Eur J Med Chem* **2008**, 43(10), 2189 - 2196.
[13] MO Agwara; PT Ndifon; MK Ndikontar. *Bull. Chem. Soc. Ethiopia*, **2004,** 18(2), 143-148.
[14] IV Morozov; VN Serezhkin; SI Troyanov. *Russ Chem B*+, **2009,** 58(12), 2407-2417.

[15] GRA Wyllie; OQ Munro; CE Schulz; WR Scheidt. *Polyhedron*, **2007,** 26(16), 4664-4672.
[16] MAS Goher; FA Mautner. *Polyhedron* **1995**, 14(11), 1439-1446.
[17] G Lazari; TC Stamatatos; CP Raptopoulou; V Psycharis; M Pissas; SP Perlepes; AK Boudalis. *Dalton Trans*, **2009,** 3215-3221.
[18] Z-L Chen; C-F Jiang; W-H Yan; F-P Liang; SR Batten. *Inorg Chem*, **2009**, 48, 4674-4684.
[19] CD Tabong; DM Yufanyi; AG Paboudam; KN Nono; DB Eni; MO Agwara. *Adv Chem*, **2016,** Volume 2016.
[20] FT Chimaine; DM Yufanyi; ACB Yuoh; DB Eni; MO Agwara. *Cogent Chem*, **2016,** 2, 1253905.
[21] C Amah; AM Ondoh; DM Yufanyi; DSY Gaelle. *Int J Chem*, **2015,** 7(1), 10-20.
[22] ACB Yuoh; MO Agwara; DM Yufanyi; MA Conde; R Jagan; KO Eyon. *Int J Inorg Chem*, **2015**, Article ID 106838, 8 pages.
[23] DYG Sado; MO Agwara; MD Yufanyi; J Nenwa; R Jagan. *Inorg Nano-Met Chem*, **2017**, 1-8.
[24] DSY Gaëlle; DM Yufanyi; R Jagan; MO Agwara. *Cogent Chem*, **2016,** 2, 1253201.
[25] WHO, Geneva, Switzerland, **2014**.
[26] J Tanwar, S Das, Z Fatima and S Hameed, Interdisciplinary Perspectives on Infectious Diseases, **2014,** 2014, Article ID 541340.
[27] B Spellberg; R Guidos; D Gilbert; J Bradley; HW Boucher; WM Scheld; JG Bartlett; J Edwards; the Infectious Diseases Society of *Clin Infect Dis*, **2008**, 46(2), 155-164.
[28] N Beyth; Y Houri-Haddad; A Domb; W Khan; R Hazan. Evidence Based Complementary and Alternative Medicine. **2015**, 2015, Article ID 246012.
[29] V Kandi; S Kandi. *Epidemio Health*, **2015,** 37, Article ID, e2015020
[30] SS Massoud; FA Mautner; M Abu-Youssef; NM Shuaib. *Polyhedron*, **1999,** 18(1), 2287-2291.
[31] E Czubacka, R Kruszynski and T Sieranski, Struct Chem, **2012**, 23(2), 451-459.
[32] S Triki, F Thetiot, J-R Galan-Mascaros, JS Pala and KR Dunbar, *RSC Adv*, **2001**, 25, 954 - 958.
[33] E Czubacka; R Kruszynski; T Sieranski. *J Struct Chem*, **2012**, 23(2), 451–459.
[34] PT Ndifon; MO Agwara; AG Paboudam; DM Yufanyi; J Ngoune; A Galindo; E Alvarez; A Mohamadou. *Transition Met Chem*, **2009**, 34, 745-750.
[35] MO Agwara; MD Yufanyi; JN Foba-Tendo; MA Atamba; DT Ndinteh, *J Chem Pharm Res*, **2011**, 3(3), 196-204.
[36] TG Balicheva; IV Pologikh; DI Kovachev; AJ Statelova. *Russ. J Inorg Chem*, **1975,** 20, 87 - 90.
[37] TG Balicheva; IV Pologikh, *Russ J Inorg Chem*, **1975,** 20(12), 1769-1773.
[38] MO Agwara; JN Foba-Tendo; A Colette; DM Yufanyi; NB Ndosiri. *Res J Pharm, Biol Chem Sci*, **2012,** 3(3), 95.
[39] CD Tabong; AM Ondoh; DM Yufanyi; J Foba. *J Mater Sci Res*, **2015**, 4(4), 70-81.
[40] ZH Chohan; KM Khan; CT Supuran; *Appl Organomet Chem*, **2004,** 18(7), 305-310.
[41] R Shakru; NJP Subhashini; SK Kumar; Shivaraj. *J Chem Pharm Res* **2010**, 2(1), 38-46.
[42] PT Ndifon; MO Agwara; NJ Ngu; DM Yufanyi; PG Awawou; LD Nyamen. *Res J Chem Env*, **2010,** 14(2), 50-54.
[43] ZH Chohan; H Pervez; A Rauf; CT Supuran. *Met Based Drugs*, **2002**, 8(5), 263–267.