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Synthesis and characterization of tetra amide macro cyclic metal-complex with transition metals and its antimicrobial property

Giriraj S. Mandloi[1], Smita Joshi[2], Surendra Sarsaiya[3] and Sulbha Amlathe[1*]
[1]Department of Applied Chemistry, UIT, Barkatullah University, Bhopal, MP, India
[2]Department of Chemistry, Govt. Geetanjali Girls' P.G. (Autonomus) College, Bhopal, MP, India
[3]Bioresource Institute for Healthy Utilization and International Research Laboratory, Medical University, Zunyi, China
samlathe97@gmail.com

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Abstract

Synthesis as well as complexes characterization [M (L^1) Cl_2], Ni (II), M=Cobalt, Nickel, Cupper, and Zinc; and ligand (L^1) was examined by FE-SEM/EDS, UV-Visible, FT-IR and XRD. The L^1 shown to be matched with tetra amide divalent transition metals giving precipitates upon self-assemblage at 0^0C. The powder XRD and FT-IR maintained the continuation of a complexion with transition metal cations indicates the formation of self–assembled over C-H... O; O-H…O interface of the termination dicarboxylic acids. The complexes were screened out for the antimicrobial activity by disc diffusion agar technique. The potency of compound [M (L^1) Cl_2] was tested against the bacteria such as E.coli and S.aureus and fungi (A. niger and C. albicans) strains. Ampicilline applied as reference for bacteria and fluconazole in case of fungi. The Copper and Nickel metal complex showed the highest in vitro antibacterial action (Escherichia coli and Staphylococcus aureus) as related to the standard drug while the metal complexes were less effective antifungal activity against test fungi (A. niger and C. albicans). Finding revealed that metal multiplexes from the synthesized compounds, which is high potential for the industry and environment.

Keywords: Self assembles, Bolaamphiphiles, rigid rod, antimicrobial activity.

Introduction

After a duo years of general research work in many laboratories all-inclusive, macrocyclic chemistry is an ingrained and the highly documented branch of science. Amide have considered a basic stone for the edifice of modern macrocyclic modern chemistry[1]. The macrocyclic legends have hollow with N-H group have an intensive area of study with the numerous transition metals[2-4]. Macrocyclic molecules containing with different ions like transition metals in adjacent is measured imperative growing effectiveness substrate[5-7]. Macrocyclic metal complexes are also applying for biological fields such as antimicrobial, antifertility, antimalarial, anticancer, antiviral and anti-HIV activities[8-13]. Chandra and Gupta[14], reported the transition macrocyclic developments with a new macrocyclic tetradentate nitrogen supporter legend, that give upsurge to ecological, industrial or healthiness-related possible application[15-19]. Many complexes possessing N-H assembly all together consequences into the gel or solid constituents[20]. The robust dimeric COOH-COOH interface in these particles remarkably provides a variety of elevations for example rod, knots, and helix etc., thus the dicarboxylic mixtures possessing various possible applications, we inspired to synthesis varieties of around new macrocyclic molecules containing N-H group diester-dicarboxylic compounds, following the desymmetrization method with a view to enriching these versatile organic molecules. Carboxylic acid is being the multidentate ligand, their coordination with metallic ion primes into the verities of metal developments. The transition metal complexes have played an essential role in a huge amount of widely differing biological procedures. Many of these progressions are necessities, in that only convinced transition metal (ions) in definite oxidation positions that can carry about the essential macrocyclic structural condition.

Recently, the tetra-amide base complexes have been reported to show a multiplicity of biological actions, which is accountable for various antibacterial, antifungal activities. They formed a novel motivating class of macro cyclic complexes that has been popularized used in the coordination chemistry of transition, and main group elements.

The present investigation was mainly focused on the synthesis of a series of compounds containing tetra amide divalent transition metals and to evaluate their antimicrobial potency.

Materials and methods

Materials, instruments and reagents: Chemicals are obtained from Aldrich and Corporation, India. The melting points were determined routinely in open capillaries, the morphology (FE-SEM/EDS) was performed on a Model JOEL JSM-5600, Japan, the microanalyses of the compounds were completed using an Elemental analyzer (HITACHI CHNS/O), Germany at CSIR, AMPRI, Bhopal. Mass examination was done via electron sprig ionization (ESI^+) procedure on water QT micro-mass spectrometer system. FT-IR bands were verified by means of KBr bits on a PerkinElmer band GX FT-IR spectrophotometer. A concentrate XRD (X-ray diffraction) pattern of dehydrated trials was chosen by the reflection system on a Rigaku diffractometer (Model: RINT 2000) via d-space elongated alongside multi-layer optics monochromatic Cu Ka radioactivity (50 kV,40 mA). The molar conductance of compact divalent shift metal developments in DMF (10^{-3} M) was precise by means of conductometer; Sybron-Barnstead (Meter- PM.6, E = 3406). The bacteria *S. aureus, E. coli* and fungus like *A. niger* and *C. albicans* were obtained from the Department of Microbiology at BU, Bhopal, M.P., India.

Synthesis of Ligand (L^1): The outline for the preparation of diester-based bolaamphiphiles is shown in Scheme-1[20].

Development of metal complex [M (L^1) Cl_2]: A mixture of L^1 (1.7g, 0.005mmol) and ethylene diamine (0.335ml, 0.005mmol) liquified in 50ml ethanol was magnetic enthused for around one hour. A warm ethanolic resolution of the appropriate metal chloride (0.0025mmol) was then added. The combination was stimulated with moderate heating (60-90°C) for 5h. cooling up gave a solid colored swift complexes was sieved off, wash away several times by cold ethanol and dehydrated underneath of vacuum.

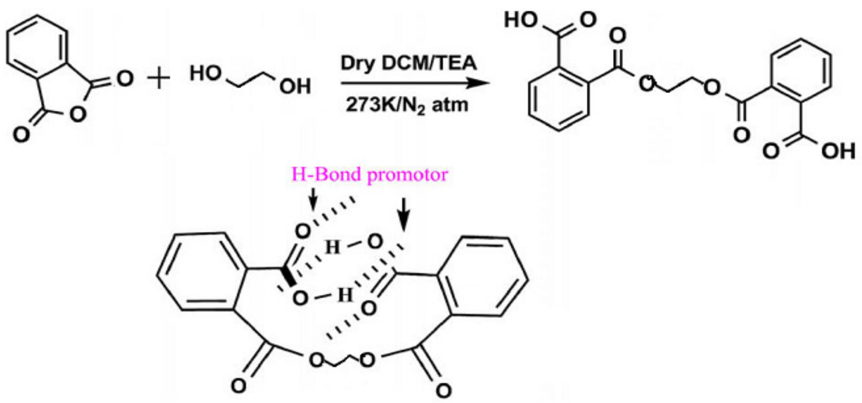
Preservation of test cultures: Fungal culture (*A. niger* and *C. albicans*) and bacterial culture (*E. coli* and *S. aureus*) were procured from the Department of Microbiology at BU, Bhopal, M.P., India for the research study. Strains were preserved on potato dextrose agar and nutrient agar media plates and tubes at 37°C and 28°C, respectively.

Filter paper disc diffusion plate assay: The experiments of antimicrobial activity were conducted using filter paper disc diffusion plate assay as described by Chandra S. et al.[21] for the fungi, the test immune serum was immersed in water. All test fungal strain deferral was dispensed into the pre-sterilized petri plates. Subsequently that melted potato dextrose agar (PDA) was dispensed into the petri plates encompassing immune serum and interchanged to combine the immune serum with homogeneously and set aside for solidification. Afterward solidification, the sterilized blotting paper round (5mm) was saturated in the dilute metal complex in diverse concentrations. The disc was dehydrated under precise temperature to eliminate additional solvent. *Fluconazole* (for fungi) and *Ampicilline* (for bacteria) and test plates nurtured at 37°C and 28°C for 24-72 hours. The outcomes were stated in relations to inhibition zone diameter. All trials were performed in triplicates.

To determine the antibacterial and antifungal activity against test microorganisms: The filter paper disc diffusion plate assay was used to regulate the antimicrobial action of metal complex [M (L^1) Cl_2] derivatives) against a test organism. The immune serum was feast over the nutrient agar plates by means of a sterile cotton gauze with the aim of obtain unchanging microbial development. Then, the organized antimicrobial metal complex [M (L^1) Cl_2] derivatives discs were kept over the lawn and pressed slightly along with control [*Fluconazole* (for fungi) and *Ampicilline* (for bacteria)]. The nurtured plates were kept at 28°C for 72 of fungi and 37°C at 24 hours for bacteria. The identical course of action was adopted for standard drugs. The movement was determined by using the technique at an attentiveness of 100μg/mL solution of synthesized [M (L^1) Cl_2] complexes. 100μg/mL solution of the standard drugs, *Fluconazole* (for fungi) and *Ampicilline* (for bacteria) were also equipped. The antimicrobial action was assessed with measured the diameter of inhibition zones in millimetre (mm). An trial was performed in triplicate and the average zone of inhibition diameter was noted.

Results and discussion

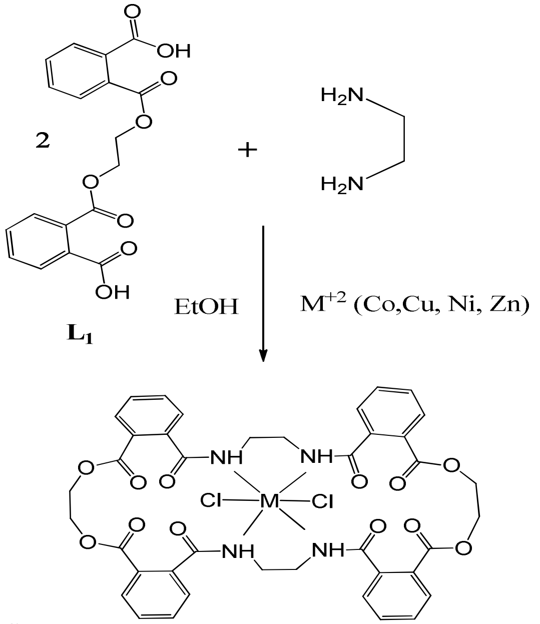
The M (L^1) Cl_2] complexes are exposed to essential analysis. The consequences are recorded with different molecular plan and melting arguments as accessible in Table-1. The consequences are attained in good contract with those intended from the optional formula. The sharp melting opinions are indicated the concentration of the preparation macrocyclic complexes is given by the scheme-2.



Scheme -1: Diester dicarboxylic Bolaamphiphiles compound with their functional role.

Table- 1: Melting point, colour, molar conductance and systematic data of the compound.

Compound	Colour	Melting point (^{0}C)	Λ_m (cm^2 Ω^{-1} mol^{-1})	Mol. Wt.	Found (Clacd.) (%)					
					M	Cl	C	H	N	O
[CoL^1 Cl$_2$]	Green, Brown	179	66	954.79	6.59 (7.23)	7.93 (8.44)	53.70 (54.72)	4.06 (5.17)	6.26 (7.20)	21.46 (22.41)
[NiL^1 Cl$_2$]	Light Blue	152	15	928.43	6.56 (7.21)	7.93 (8.52)	53.72 (54.27)	4.06 (5.17)	6.26 (7.21)	21.47 (22.39)
[CuL^1 Cl$_2$]	Dull Green	134	17	959.32	7.07 (7.1)	7.89 (8.10)	53.43 (53.89)	4.04 (4.87)	6.23 (7.11)	21.35 (22.07)
[ZnL^1 Cl$_2$]	White	240	28	961.18	6.56 (7.21)	7.93 (8.54)	53.72 (53.24)	4.06 (5.18)	6.26 (7.20)	21.47 (22.40)



Scheme-2: Synthetic rout of metal complexes.

Configuration and structure of metal developments: The formation of tetra amide macrocyclic compound of the transition metals, the ligand (L^1) was exposed to elemental examines (C, N, H and metals), FT-IR, conductance of moles with FE-SEM, to recognize their uncertain formulae in a test to explain their structures. The consequences of elemental examines are recorded in Table-1 recommend the formulae nature [M (L^1) Cl$_2$], (M=Cobalt, Nickel, Cupper, and Zinc).

Measurement of molar conductivity: The tetra amide metal developments were liquified in DMF with the molar conductivity concentrations of 10^{-3}M at 25°C were analysed. Table-1shown the conductance of molar values of the transition metal developments. Molar conductivity standards reduction series of 15–66Ω^{-1}mol^{-1}cm^2 represented that these are complexes with non-electrolytes.

Electron microscopic observation: The FE-SEM of the transition metal complexes was recorded to understand the formation of rigid rod structures. To elucidate the rigid rod structures are accountable for the coordination with the metal ions, respectively. We carried out the FE-SEM images in Figure-1 and 2 display the 1/ Copper (II) complexes upon self-assembly at room temperature. The 1/Copper (II) complex stick is nearly comparable to the carbon-based nano fibres as before described[22,23]. The metal cation developments were also self-possessed of the rigid rod. We also performed EDS to clear percentage amount of metal present in the tetra amide metal complexes. The EDS of each rigid rod shows the peaks ascribable to transition metals correspondingly. This pronouncement reinforced that the structure is essentially collected of the metal developments of Bolaamphiphiles ligand (L^1). Uniform widths of the metal-complexes rigid rod indicates that both the length of the end terminal carboxylic acids and the types of metal cations have slight effect on the structure of the rigid rod.

FT-IR and XRD analyses: The data of developments recorded in Table-2. FT-IR spectrums in Figure-3, shown the complex formation the changeable in the direction of the lesser surface of υ (N–H) group. This is recommend the harmonization from side to side the amide nitrogen [–NH cluster (N4)] and maintained by the outward show strength resonated 426-496cm^{-1} ascribed υ (M-N) and υ (M–Cl) exterior weak band rang 280-320cm^{-1} [23,24].

A pointed band observed 3182-3284cm^{-1} given to υ (N–H) subordinate amine as shown in below Table-2[25]. FT-IR band does illustrate signs of any spectrum equivalent to the free chief diamine and the hydroxyl cluster[26].

Thus, the two sets of FT-IR peaks appeared in this region indicate the presence of the terminal and the spacer COO group in all these metal complexes. The XRD outlines of the remote and dehydrated transition metals, developments upon self-assemblage at room temperature are revealed in Figure-4. Even though the strengths are moderately sharp for the reason that of the crystalline nature of the 1/Copper (II) although the intensities are relatively strong reflection peaks appear in a comparable way as the carbon-based sharp rigid rod structure. The nonappearance of strong intermittent reflection points in the minor-angle area proposes that the rod is built on no extended-range association. All the consequences of the microscopic thought, FT-IR band, and XRD examination maintained to the metal harmonization of fatal carbonyl anions take place on the organic sharp rigid rod structure.

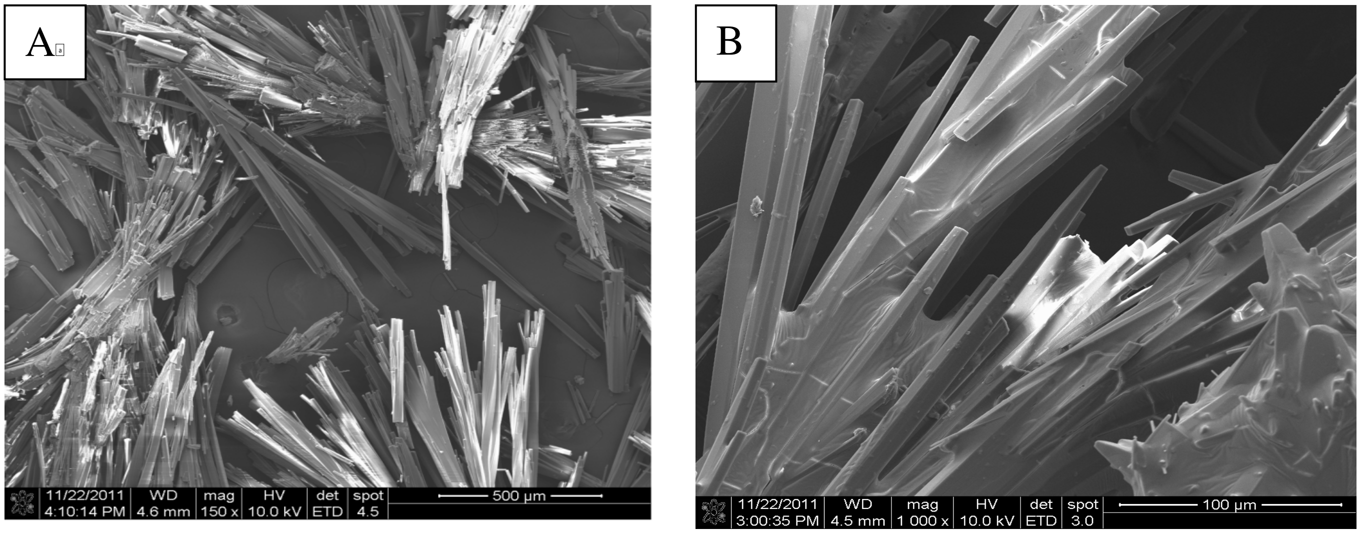


Figure-1: FE-SEM picture of (A) is Ligand L^1 and (B) is the Copper (II) complex, self-assembled at room temperature on complexation with metal ions.

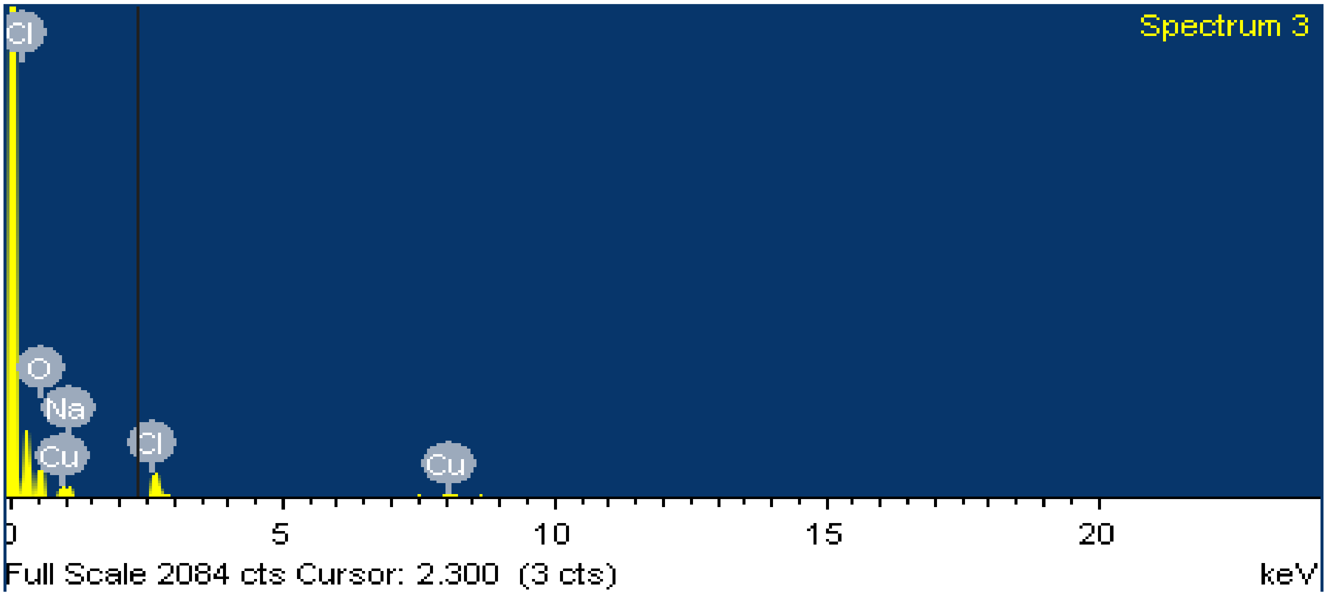


Figure-2: EDS band of the Copper (II) complex, self-assembled at ambient temperature.

Table-2: FT-IR Vibrational frequencies of the compounds.

Compound	υ (N-H)	υ (C-H)	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	υ (M-N)	υ (M-Cl)	Ring vibration
$[CoL^1 CL_2]$	3270,3200	2900	1680	1490	1240	690	440	300	1230,1015,860
$[NiL^1 CL_2]$	3300,3240	2910	1700	1500	1270	680	440	300	1225,1010,865
$[CuL^1 CL_2]$	3290,3230	2910	1690	1520	1240	660	440	300	1235,1010,855
$[ZnL^1 CL_2]$	3290,3290	2880	1700	1520	1250	660	430	320	1225,1010,850

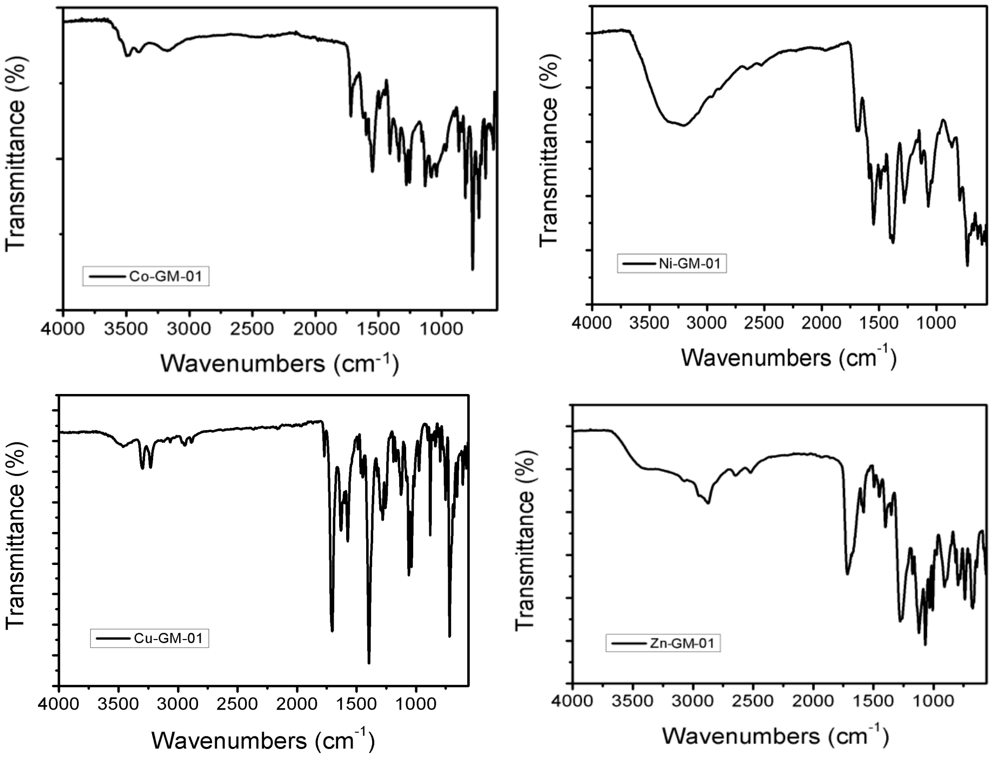


Figure-3: FT-IR spectra transition metal complexes.

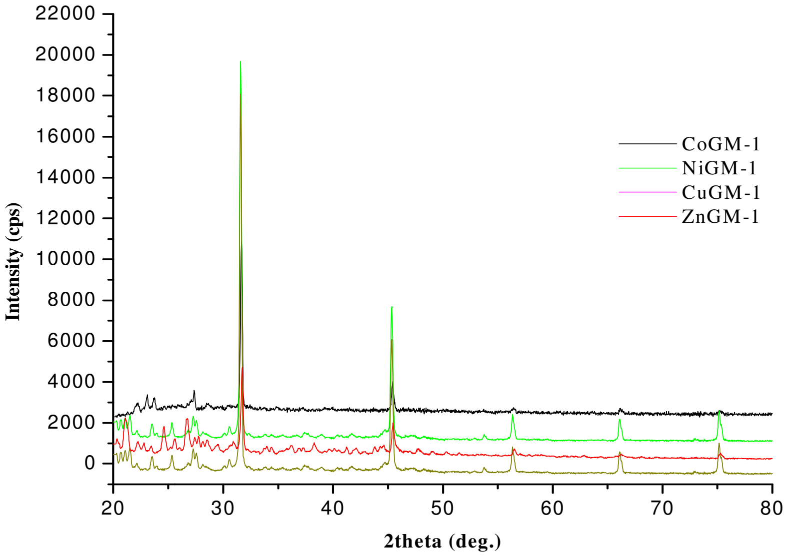


Figure-4: XRD designs of the recovered and dried transition metal complexes upon self-assembly at room temperature.

UV-Vis Spectra: The experimental sites of the absorption groups in the electric band of the transition metals, macrocyclic developments noted DMSO presented a weak strength band at 19151,26954, 14947 and 22675cm^{-1} consistent to a high rotation classification which may be assigned dependable with an octahedral situation in the area of the all transition metal complexes. However, the cobalt (II) developments exhibit two groups in the 21739, 20366 and 17953, 19157cm^{-1} areas also resemble to high spin scheme transferable transitions, correspondingly, dependable through region of the copper (II) ions. Developments, everyone presented a magnetic instant analogous to a spin permitted multifaceted. Their UV spectrum showed two separate bands arising from the geometry of the Ni (II) complex. Two spectra around 40160, 37664 and 28490, 26954 cm^{-1} and one broadband around 11150 and 11250 cm^{-1} exchangeable transition, respectively. The UV spectrum of Zn (II) complex, every show 20250, 20400 cm^{-1} sideways by the 16450, 16550 cm^{-1} respectively. This absolutely assigned to the transitions, corresponding to a distorted octahedral geometry. Their magnetic instant values additional provision the above-anticipated geometry. The high intensity bands observed around 36764 cm^{-1} for all the developments in the UV area may be allocated as a metal ligand control transmission excitation shown in Figure-5[27-28].

Antibacterial and Antifungal activity of [M (L^1) Cl_2] derivatives: The results of an *in vitro* antimicrobial activity showed that the activity of metal complex [M(L^1) Cl_2] derivatives constituents possess antimicrobial activity against the selected test organism. In the filter paper disc diffusion plate method, out of total four metal complex, the CuL^1 Cl_2 complex was verified to be greatest active against the *E. coli* display inhibition zones of 15mm which was highest among all the metal complex used in the study followed by NiL^1 Cl_2 complex showing inhibition zone of 14mm against *Escherichia coli* and *Staphylococcus aureus*. Moderate activity was shown against four metal complex with CoL^1 Cl_2 and ZnL^1 Cl_2 display inhibition zone of 13-14 mm compared to both *Escherichia coli* and *Staphylococcus aureus*, respectively. Minimum activity was shown by four metal complexes of CuL^1 Cl_2 and ZnL^1 Cl_2 exhibiting 12 mm inhibition zone against *Staphylococcus aureus*. Ampicilline and Fluconazole, used as confident controls and were verified to be less active than the metal complexes against all the test.

In case of fungi, the data shown in Figure-6 showed that out of total four metal complex shown, the NiL^1 Cl_2 complex was found to be most effective against both the test fungi (*Aspergillus niger and Candida albicans*) followed by ZnL^1 Cl_2 complex showing inhibition zone of 2mm against *Aspergillus niger*. Minimum activity was shown against four metal complex with CoL^1 Cl_2 and CuL^1 Cl_2 viewing inhibition zone of 1 mm in contradiction of both fungi respectively.

The consequences antibacterial action showed that the zone of habitation inclines to make the complexes performance as more controlling and potent antibacterial mediators, thus carnage more bacteria than the fungi.

Enlargement inhibitory effects of transition metal ions are significant against antibacterial activities. The behaviour of transition metal ions to allocate charge with the donor groups are reduced ahead chelating. The transition metal complexes are less effective anti-fungal agents than its metal complexes. The tetra-amide based macrocyclic complexes are newly reported and are tested for their antibacterial action against some bacteria corresponding *S. aureus*, and *E. coli* in which the metal complexes are less active against the two pathogenic microorganisms specifically *Aspergillus niger,* and *Candida albicans*. The transition metal ion complexes are vastly active against above two types of bacteria. *E. coli* was originating to give the details high action towards complexes, fairly they are active towards the complex. *Staphylococcus aureus (S. aureus)* was originated to be extremely active against amide complexes. The prepared compound was active towards both types of bacteria such as *Escherichia Coli and Staphylococcus aureus,* respectively.

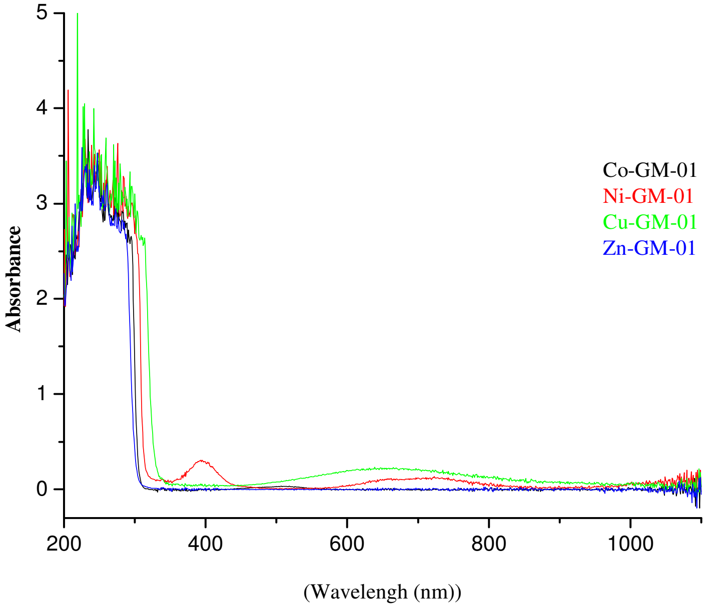


Figure-5: UV-Vis spectra transition metal complexes.

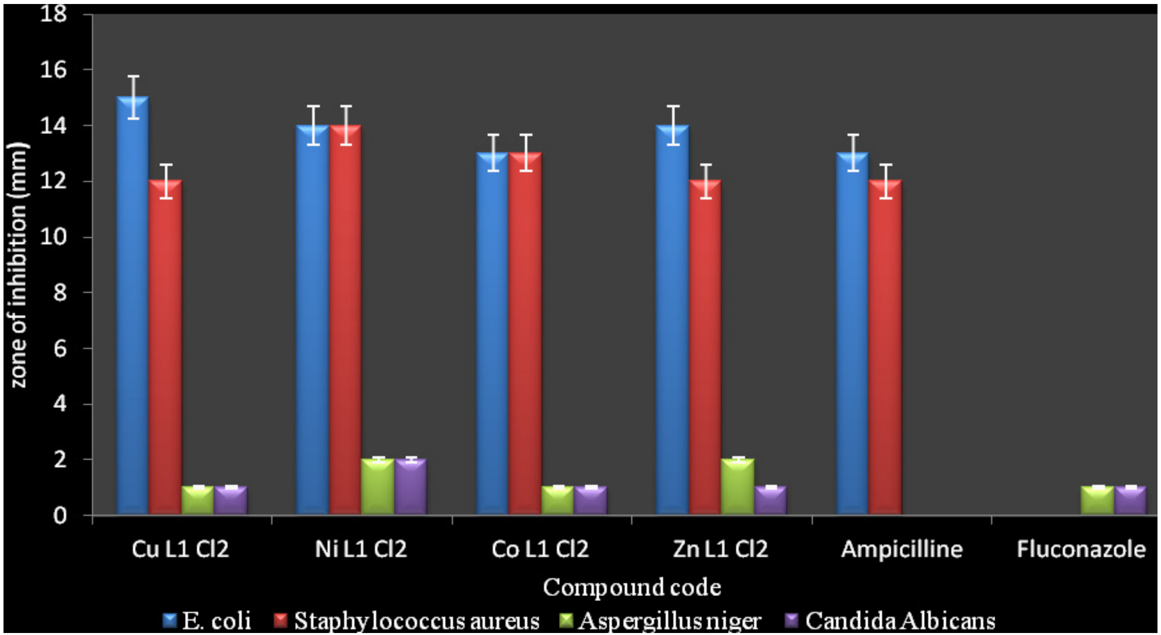


Figure-6: *In vitro* antimicrobial activity of metal complex $[M(L^1)\ Cl_2]$ derivatives against test microbes.

Escherichia Coli

Staphylococcus areas

Figure-7: Antibacterial activity of metal complex $[M\ (L^1)\ Cl_2]$ derivatives against test microbes (*E.coli and S. areas*).

Conclusion

The tetra amide macrocyclic developments make in the way with shift-metal cations, for example transition metals making through molecule self-assemblage. The FE-SEM images have been observed revealed the metal-complexes formation of rigid rod structure. In a similar manner as the rigid rods shaped from the metal complexes, the Co^{2+} were verified to shape the rigid rods by coordination with metal cations. It is concluded that in these complexes from the molecular prescription as deduced from elemental analysis. All of the verified compounds presented a noteworthy biological action against diverse types of bacteria.

Relating biological action standard and metal developments with the reference Ampicilline (an antibacterial mediator) and fluconazole (an antifungal mediator), it is perceived that: i. The biological action of transition metal complexes is reasonable in comparison with the reference used. It has less antifungal action towards test fungi. ii. The lasting metal developments have extra or less biological action that follows the direction: Nickel > Cupper ≥ Zinc > Cobalt.

Acknowledgments

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