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Synthesis and characterization of a new macrocyclic ligand and its cobalt(II), copper(II) and zinc(II) complexes

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Abstract

The synthesis of a new ligand, N_4 Tetra (Methyl Azomethine)-Diethylene Hydrazide (TMADEH), was carried out through the condensation of 1,2-diacetylhydrazine with ethylenediamine. The metal complexes of TMADEH were prepared by reacting ligand with Co^{2+}, Cu^{2+} and Zn^{2+}. The structures of the ligand and its complexes were confirmed using various techniques including FT-IR, UV-VIS, ^{1}H-NMR, ^{13}C-NMR, elemental analysis, electrical conductivity and atomic absorption spectroscopy.

It was found the ligand acts as a tetra-aza ligand and the metal complexes have the formulas [Co (TMADEH)Cl_2], [Cu (TMADEH)$(H_2O)_2$]Cl_2 , [Cu (TMADEH)$(H_2O)_2$]Cl_2 with metal ratio (1:1) and octahedral structures.

Keywords: Macrocyclic ligand, metal complexes,1,2-Diacetylhydrazine, Schiff bases**,** Ethylenediamine.

Introduction

The coordination chemistry of macrocyclic ligands has emerged as a rapidly expanding field of research, owing to their significant roles in chemistry and biochemistry. Historically, coordination chemistry was primarily associated with the complexation of metal cations. However, chemists worldwide are now extensively exploring the coordination chemistry of macrocycles, porphyrins and related systems to harness their benefits. This exploration has led to the development of a specialized area within coordination chemistry known as macrocyclic chemistry[1,5,9,12]. Macrocyclic compounds exhibit unique and fascinating chemical properties, offering a diverse array of donor atoms, ionic charges, coordination numbers and geometries in their resulting complexes.

It is not an exaggeration to state that macrocyclic ligands are central to life, particularly in their roles in elucidating and explaining mechanisms such as photosynthesis, oxygen transport in mammalian and other respiratory systems and their potent activity as DNA binders with significant potential in antitumor therapy[4,8].

These compounds have garnered significant attention due to their importance as anticancer, antibacterial and antifungal agents. Additionally, they play crucial roles in catalytic applications and in oxidation and reduction processes[4,6,7,11].

In this study, we aim to synthesize and characterize the complexes of Co (II), Cu (II) and Zn (II) with the new macrocyclic ligand Tetra (Methyl Azomethine)-Diethylene Hydrazide (TMADEH).

Material and Methods

Materials and Apparatus: All the used chemicals in this work were produced from BDH, Aldrich and Merck and were used without further purification.

NMR spectra were recorded using a Brucker instrument (400 MHz) spectrometer. Chemical shifts were reported in (δ) ppm relative to tetramethylsilane (TMS). Data were reported as follows: chemical shift, multiplicity, coupling constant (Hz), integration and assignment. FT-IR spectra (ν, cm^{-1}) were recorded on a JASCO Spectrum (FT–IR 4100) spectrometer using KBr pellets. UV-Vis spectra were measured by using Jasco-V630-UV-Vis at the wavelength range (200–1000 nm), using match quartz cells (1 cm) and DMSO as a solvent. Atomic absorption spectroscopy data was recorded on a novAA- 400.

Synthesis of the ligand Tetra (Methel Azometine)-Di ethelene hydrazide (TMADEH): An ethanolic solution (60 ml) of 1,2-Diacetylhydrazine (0.118 g, 1 mmol) and an ethanolic solution (30 ml) of ethylenediamine (0.067 ml, 1 mmol) were mixed slowly under constant stirring. This mixture was refluxed at 75 °C for 48 h in the presence of a few drops of concentrated HCl (pH =8). On cooling, a white-colored compound precipitated out.

This was filtered, washed with cold EtOH and dried under vacuum over P_2O_5. Yield≈61.69 %; m.p. > 300℃. Anal. Calcd. For $C_{12}H_{24}N_8$ (FW 280.374): C, 51.40; H, 8.62; N,39.9 %. Found: C, 49.32; H, 8.11; N, 38.01 %. The preparation and structural formula of the ligand are shown in fig. 1.

Synthesis of complexes: A methanolic solution (15 ml) of the ligand (0.140 g, 0.5 mmol) and a methanolic solution (20 ml) of the required metal salt ($CoCl_2$, $CuCl_2$ and $ZnCl_2$) (0.5mmol) were mixed together under constant stirring. This reaction mixture was refluxed at 65°C for 27h. After 27 h of stirring, the volume of the solution reduced to 10 ml and filtered.

The solid resultant was obtained and washed with hot methanol (3 × 3 ml), followed by diethyl ether, then dried under vacuum over P_2O_5 and weighted**.** Structural formula of the complexes is shown in fig. 2.

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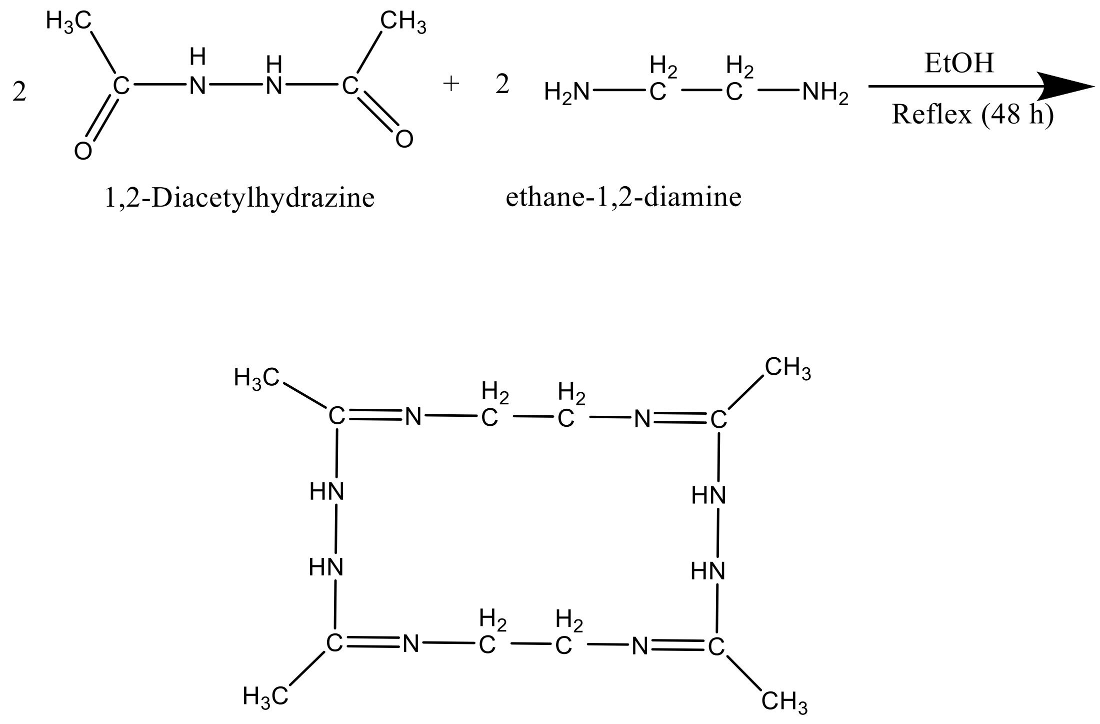

3,8,11,16-tetramethyl-1,2,4,7,9,10,12,15-octaazacyclohexadeca-3,7,11,15-tetraene
(TMADEH)

Fig. 1: Preparation and structural formula of the ligand.

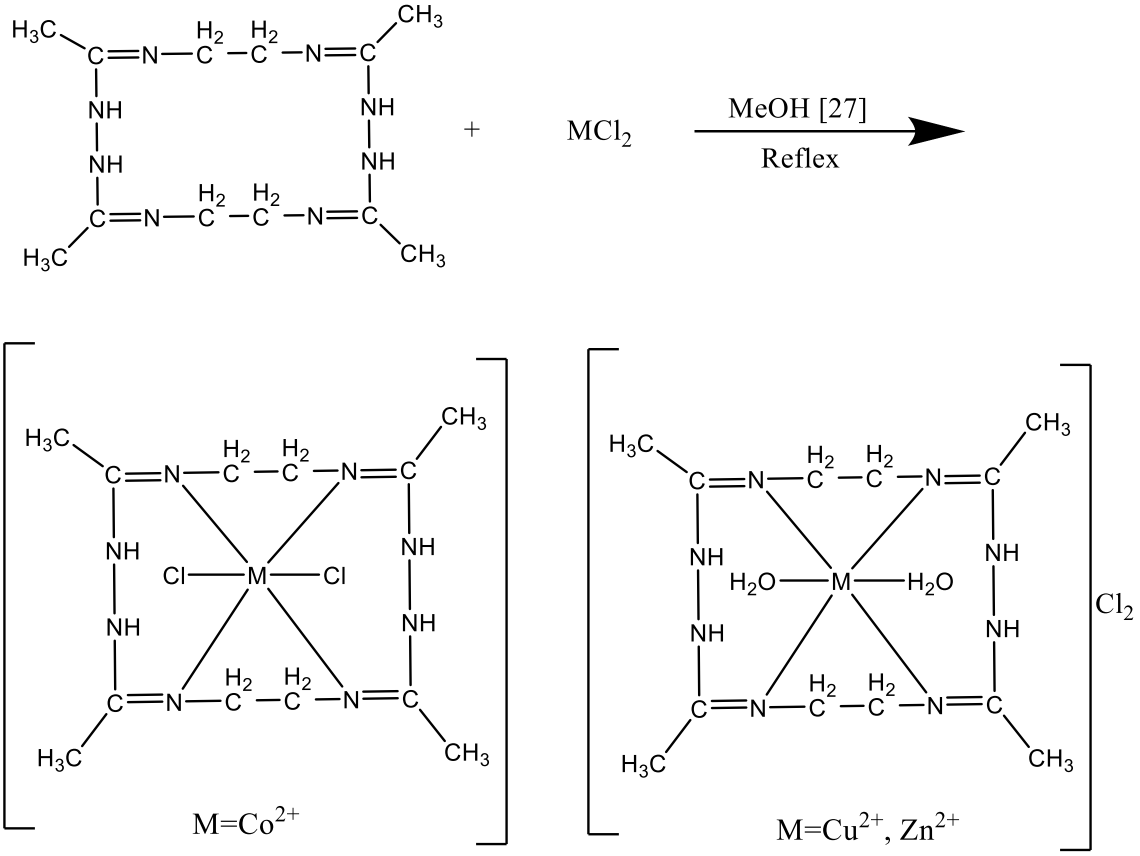

Fig. 2: The structural formula of the metal complexes

Results and Discussion

NMR characterization: TMADEH compound was characterized using H-NMR and C-NMR.

The ^{1}H-NMR spectrum of the ligand (TMADEH) gave no signal corresponding to primary amine protons. ^{1}H NMR: (400 MHz, DMSO) δ 1.845 (S, 8H), 3.109 (S, 12H), 8.49 (S. 4H) ppm. ^{13}C NMR: (125 MHz, DMSO): δ 20.95, 36.96168.60, ppm. Fig. 3 and fig. 4 demonstrate the obtained spectra.

FT-IR of TMADEH ligand and its complexes: The IR spectrum of the free ligand exhibited no bands corresponding to the primary amine or a free keto group. This suggests complete condensation of the amino groups with the keto groups. The bands at 1636 and 1597 cm^{-1} are due to ν(C=N) vibrations of the azomethine, the bands at 3185 cm^{-1} belong to N-H. The strong and sharp absorption bands appear in the regions 2925–3010 and 1385-1348 cm^{-1} in all spectra due to CH_3, CH_2 stretching and bending vibrations respectively. In metal complexes spectra, the position of the ν(C=N) band shifted by 14–35 cm^{-1}. This indicates coordination through the N atoms of the imine groups. The most important IR data of TMADEH ligand and its complexes are summarized in table 2.

UV-Vis characterization: The electronic spectra of TMADEH ligand and its complexes show the electronic transformation between energy levels. Figures 13-18 present the UV-Vis of TMADEH ligand and its complexes.

Table 1
The physical properties of the prepared compounds

Comp	Formula	M (g.mol^{-1})	Color	Melting point ^{0}C	Yield (%)
TMADEH	$C_{12}H_{24}N_8$	280.374	white	>300	61.693
[Co (TMADEH)Cl_2]	$CoC_{12}H_{24}N_8Cl_2$	410.212	blue	245	68.44
[Cu (TMADEH)$(H_2O)_2$]Cl_2	$CuC_{12}H_{26}N_8OCl_2$	432.989	dark yellow	265	57.57
[Zn (TMADEH)$(H_2O)_2$]Cl_2	$ZnC_{12}H_{26}N_8OCl_2$	452.654	white	240	54.32

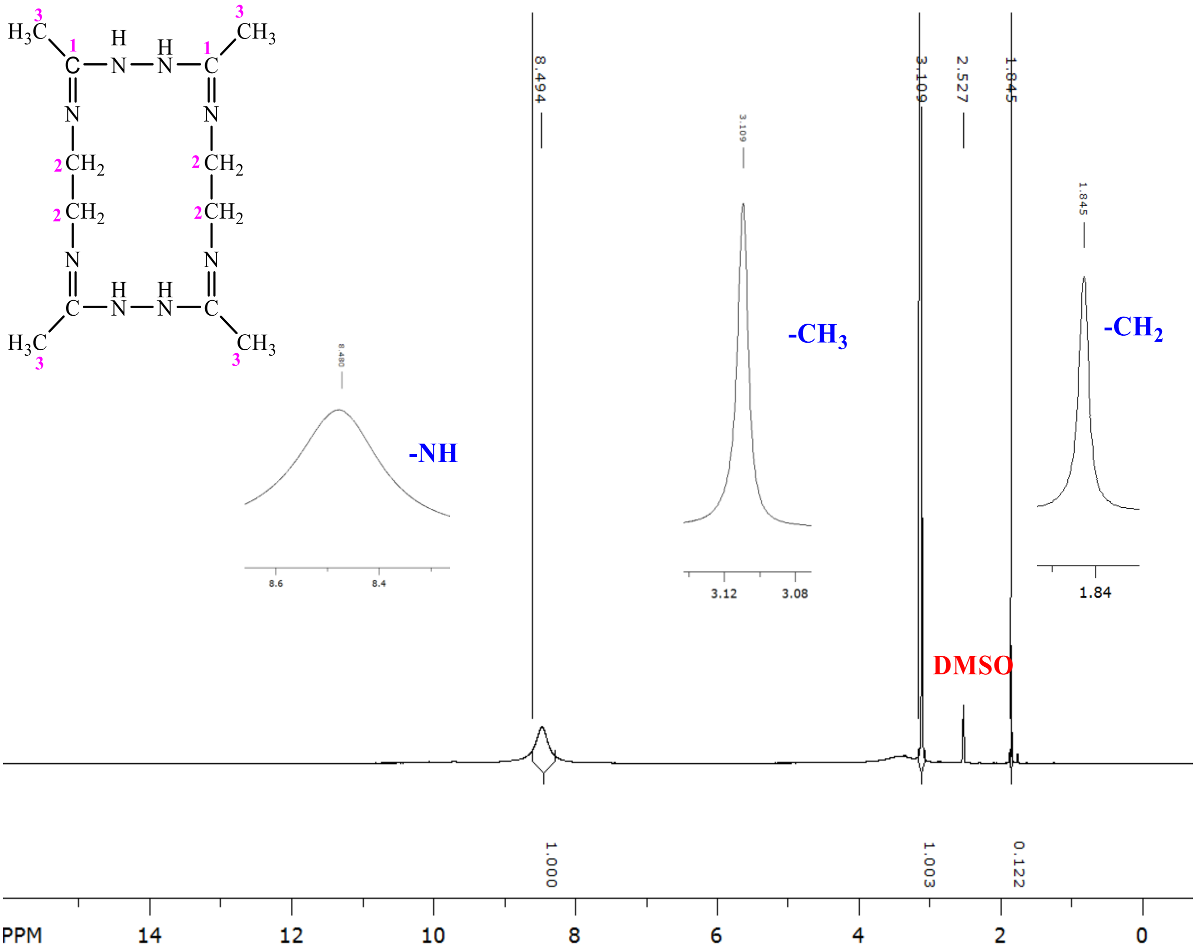

Fig. 3: ^{1}H NMR spectrum of TMADEH

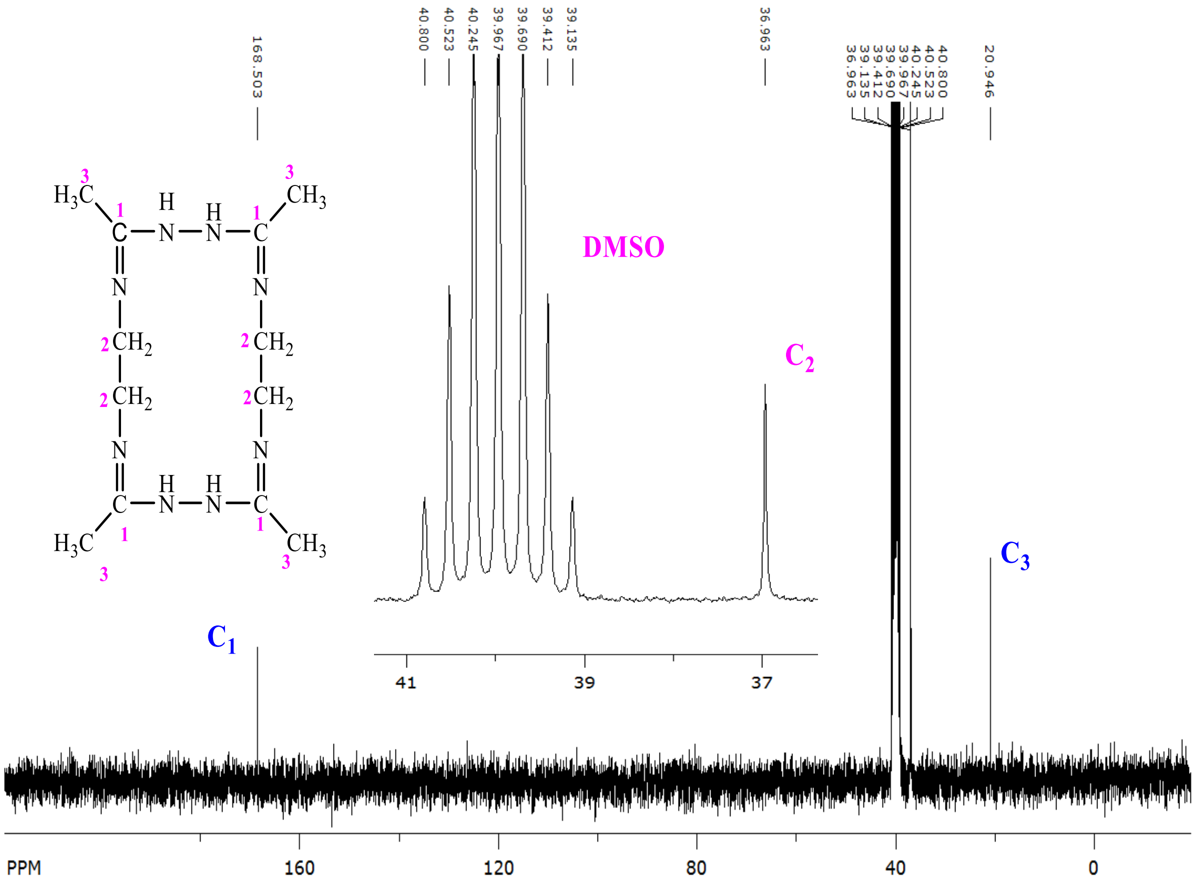

Fig. 4: ^{13}C NMR spectrum of TMADEH

Table 2
The absorption bands of TMADEH and its complexes

Comp.	N-H ῡ(Cm^{-1})	(C=N)$_1$ ῡ(Cm^{-1})	(C=N)$_2$ ῡ(Cm^{-1})	C-N-H ῡ(Cm^{-1})	CH$_3$ bend ῡ(Cm^{-1})	CH$_2$ bend ῡ(Cm^{-1})
TMADEH	3185	1636	1597	1506	1385	1348
[Co (TMADEH)Cl$_2$]	3196	1601	1583	1509	1383	1340
[Cu (TMADEH)(H$_2$O)$_2$]Cl$_2$	3176	1630	1576	1504	1385	1319
[Zn (TMADEH)(H$_2$O)$_2$]Cl$_2$	3180	1605	1583	1504	1376	1339

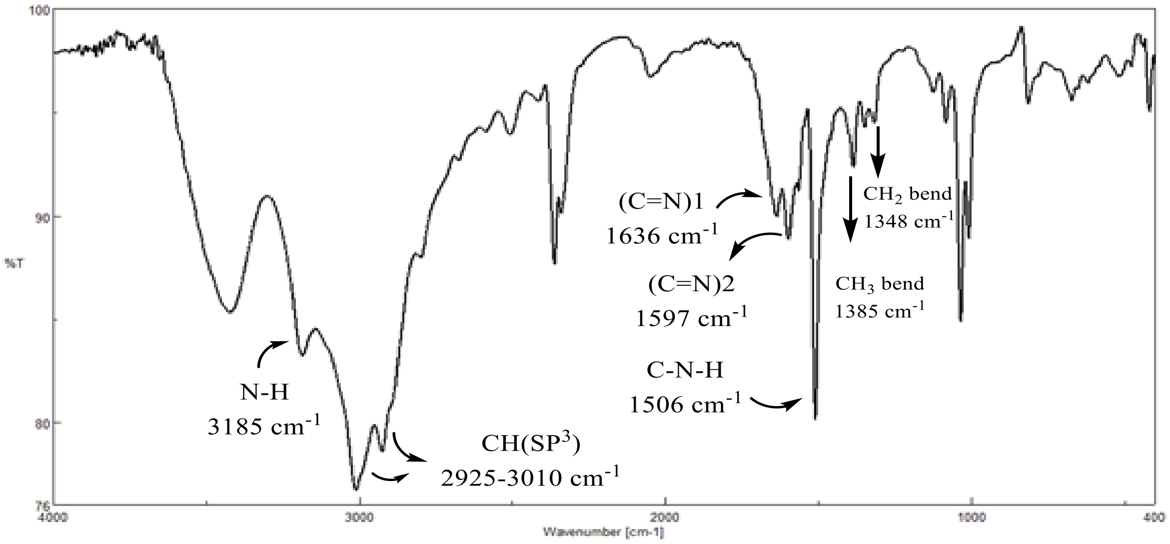

Fig. 5: FT-IR spectrum of TMADEH

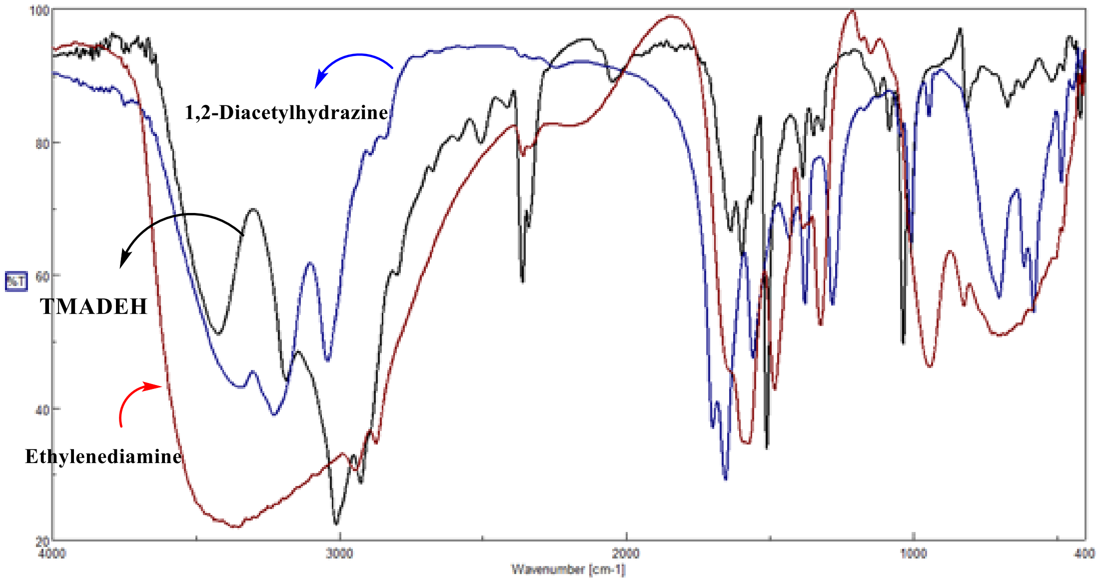

Fig. 6: FT-IR spectrum of TMADEH compared with 1,2-Diacetylhydrazine and Ethylenediamine

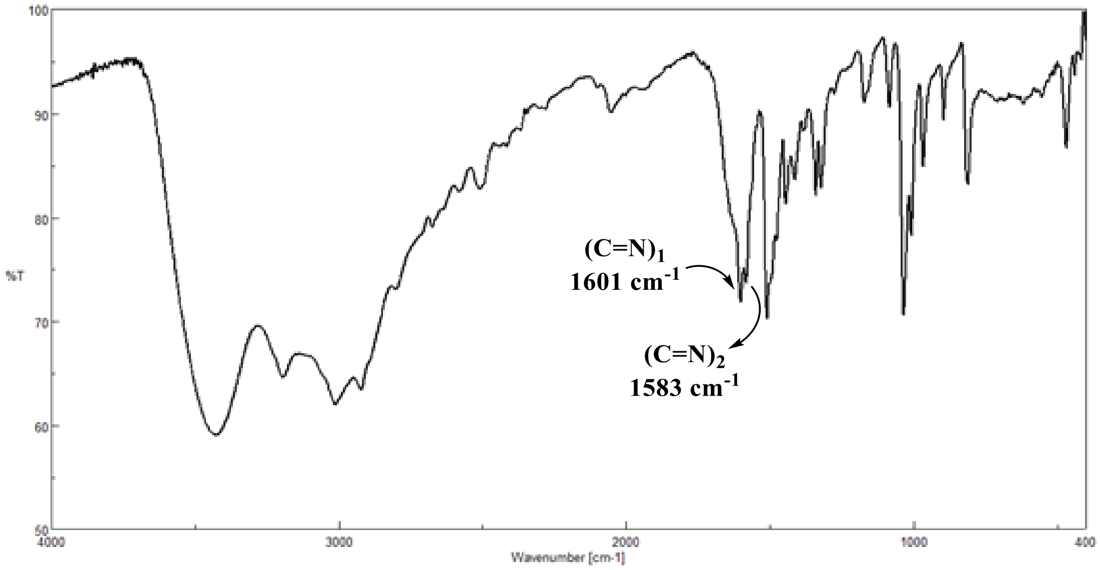

Fig. 7: FT-IR spectrum of [Co (TMADEH)Cl_2]

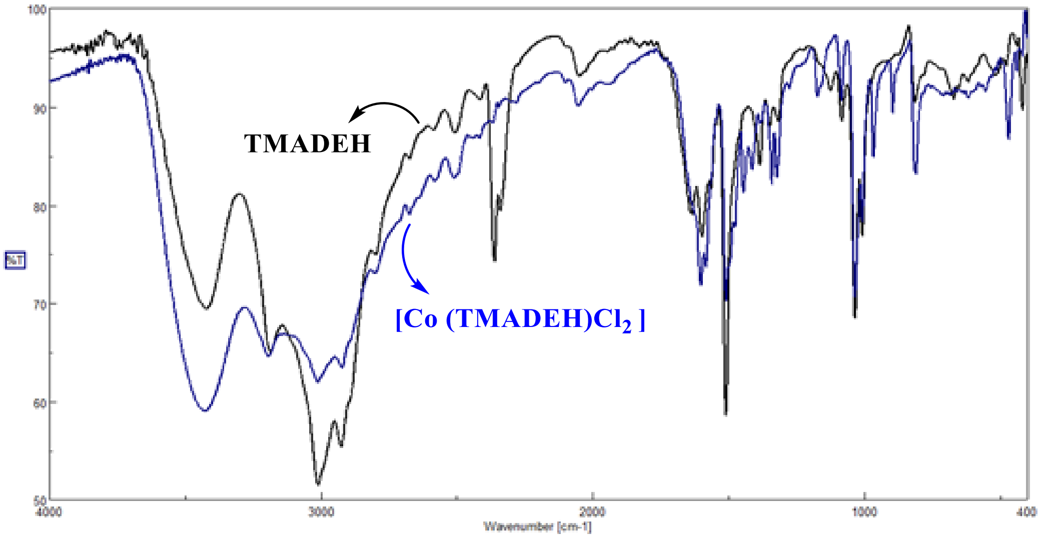

Fig. 8: FT-IR spectrum of [Co (TMADEH)Cl_2] compared with TMADEH

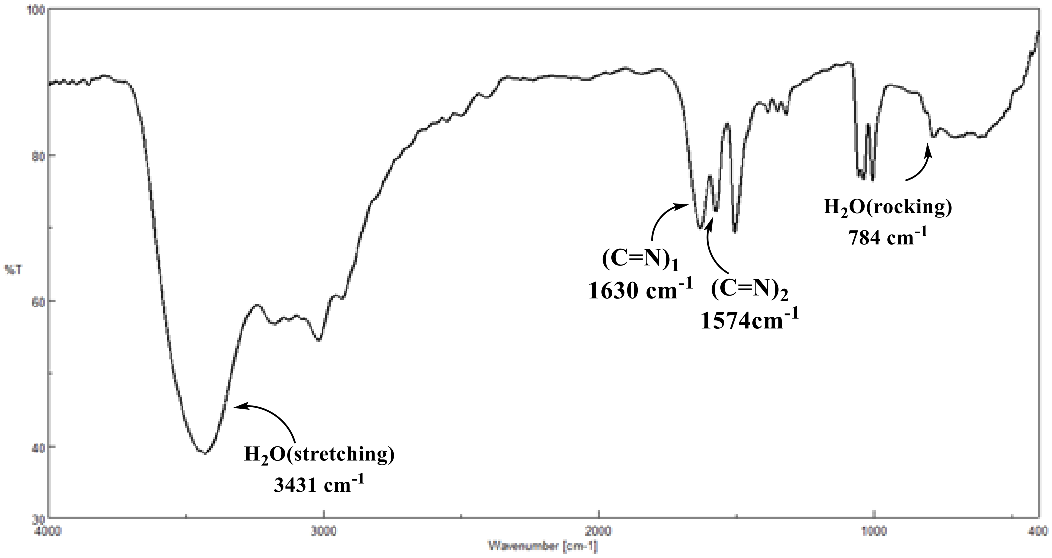

Fig. 9: FT-IR spectrum of [Cu (TMADEH)$(H_2O)_2$]Cl_2

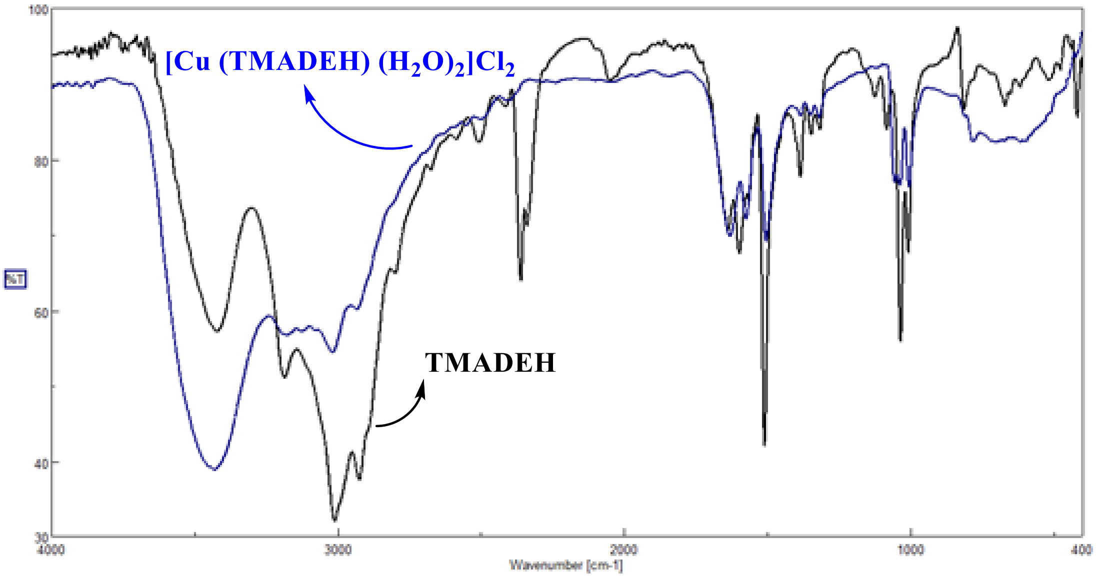

Fig. 10: FT-IR spectrum of [Cu (TMADEH)$(H_2O)_2$]Cl_2 compared with TMADEH

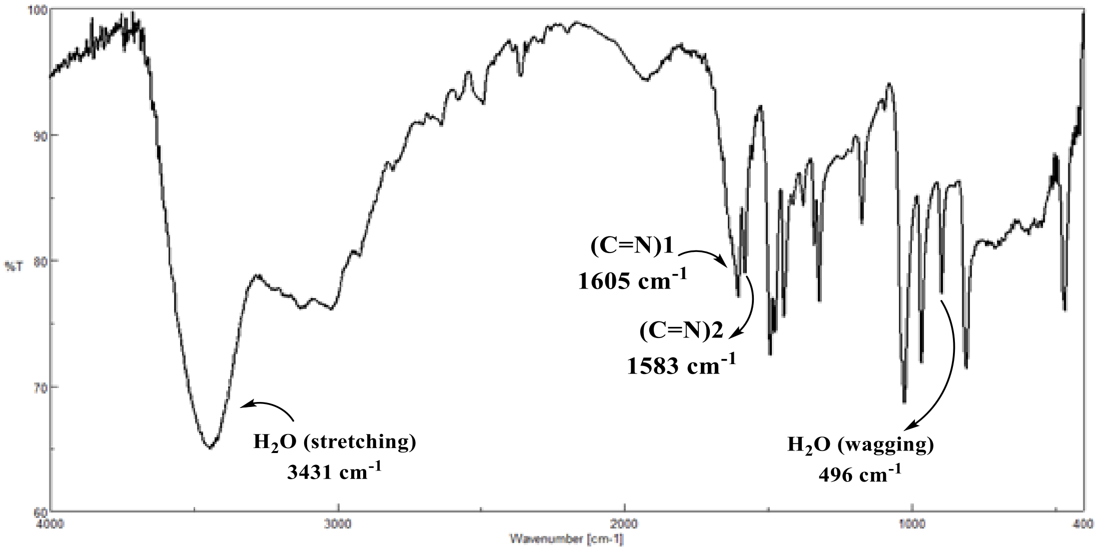

Fig. 11: FT-IR spectrum of [Zn (TMADEH)$(H_2O)_2$]Cl_2

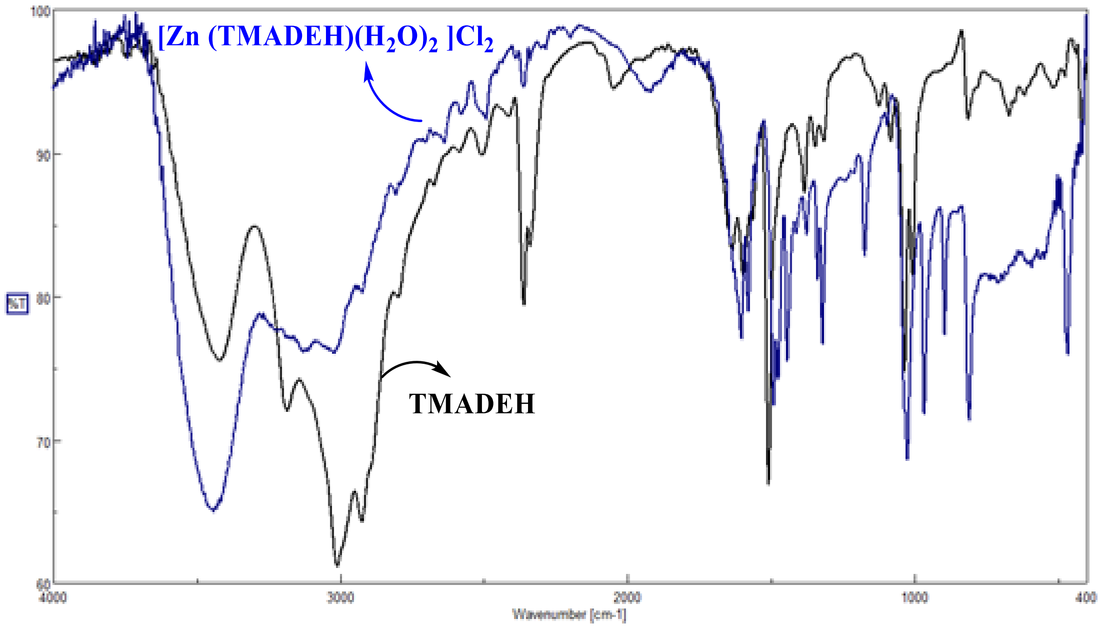

Fig. 12: FT-IR spectrum of [Zn (TMADEH)$(H_2O)_2$]Cl_2

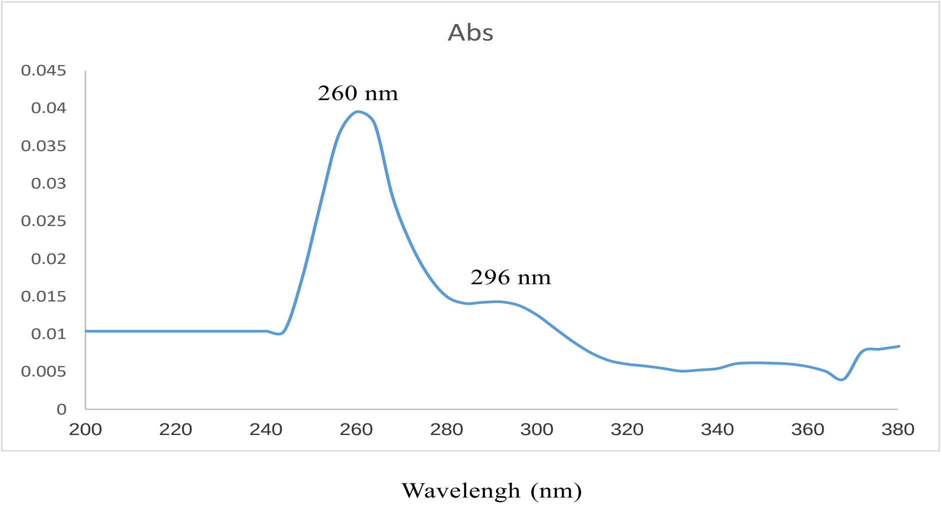

Fig. 13: UV spectrum of TMADEH

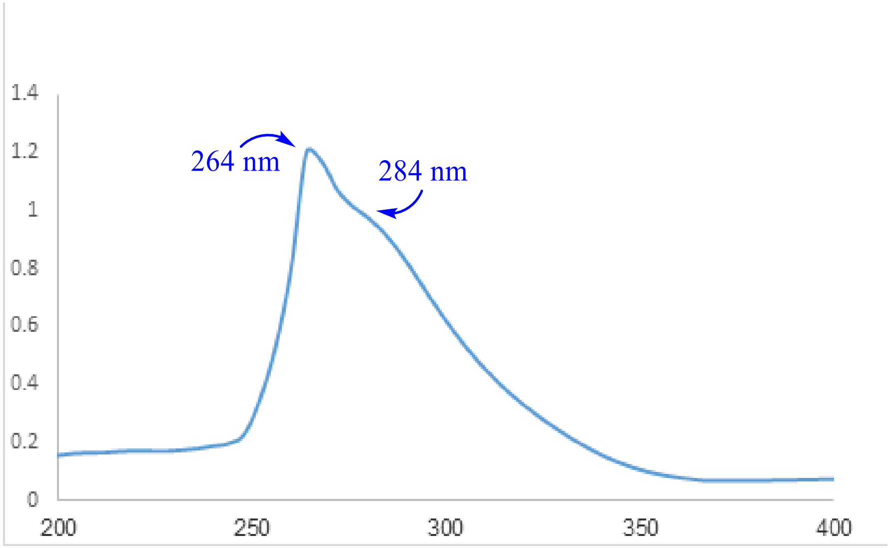

Fig. 14: UV spectrum of [Co (TMADEH)Cl_2]

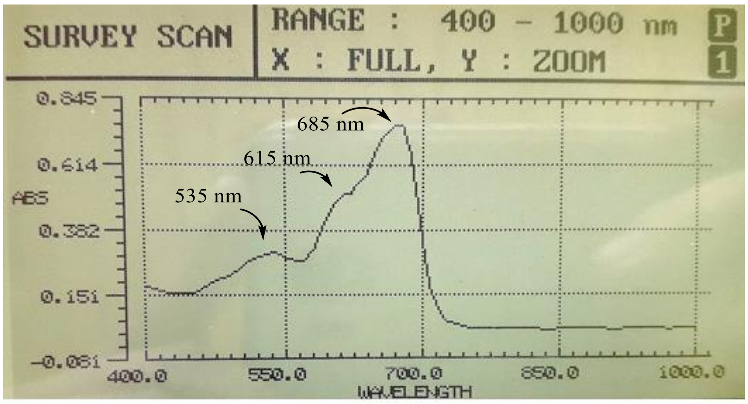

Fig. 15: VIS spectrum of [Co (TMADEH)Cl_2]

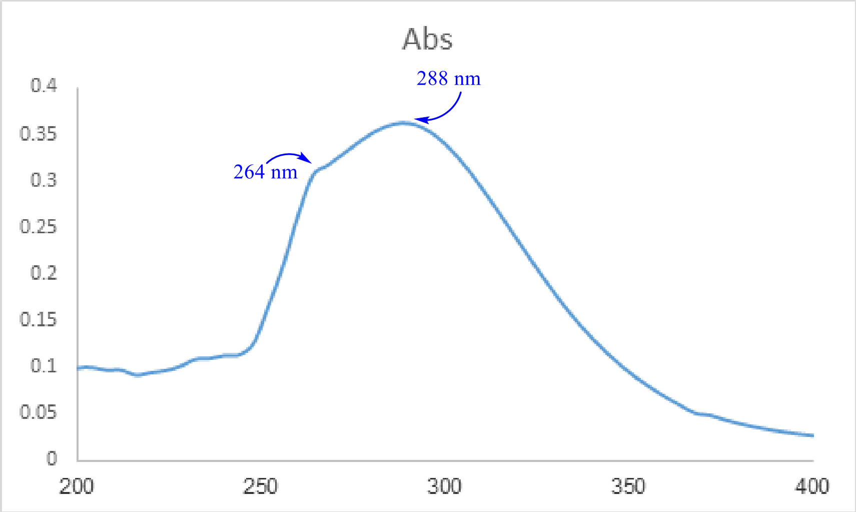

Fig. 16: UV spectrum of [Cu (TMADEH)$(H_2O)_2$]Cl_2

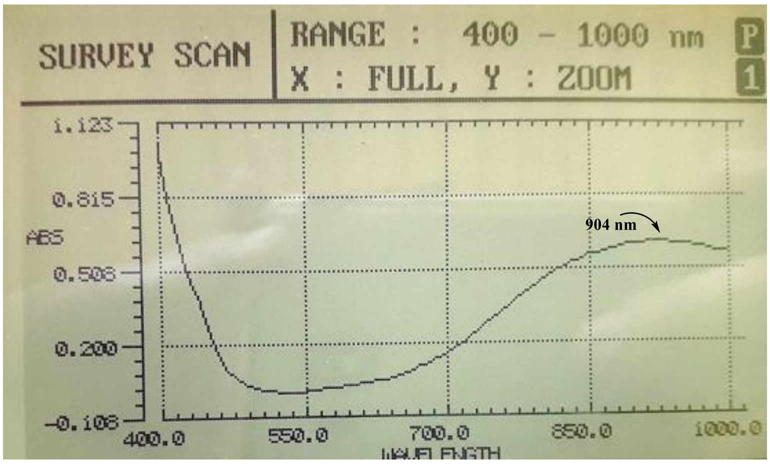

Fig. 17: VIS spectrum of [Cu (TMADEH)$(H_2O)_2$]Cl_2

The obtained data from UV-VIS spectra are arranged in the table 3.

Elemental analysis for ligand: The macrocyclic ligand was subjected to elemental analyses. The results of elemental analyses (C, H and N) of ligand are given in table 4.

Atomic absorption spectroscopy: Atomic absorption spectroscopy (AAS) was used to determine the metal content in the prepared complexes and the table 5 shows the results of atomic absorption spectroscopy.

Antibacterial Activity Study: The antibacterial efficacy of the synthesized compounds was assessed against *Pseudomonas aeruginosa* and *Staphylococcus aureus*, with *Gentamicin* used as a reference. Two different concentrations (50 and 100 mg/ml) of the compounds and gentamicin were selected for the antibacterial assay. We chose *Pseudomonas aeruginosa* and *Staphylococcus aureus* for our study due to their widespread prevalence in society and their impact on human daily life. *Pseudomonas aeruginosa* was commonly found in various environmental settings such as soil and water. Among the different strains of Pseudomonas, *Pseudomonas aeruginosa* is the most frequent cause of infections in humans leading to conditions like bloodstream and lung infections (pneumonia), as well as infections in other parts of the body following surgical procedures[10].

On the other hand, *Staphylococcus aureus* is a significant bacterial pathogen in humans, responsible for a wide range of clinical symptoms. Infections caused by *Staphylococcus aureus* are prevalent in both community and hospital settings and managing the treatment is increasingly challenging, due to the emergence of multi-drug resistant strains such as MRSA (Methicillin-Resistant *Staphylococcus aureus*)[2,3]. *Staphylococcus aureus* is found in the environment and is also a component of normal human flora, residing on the skin and mucous membranes, most commonly in the nasal area of most healthy individuals. The results of the antibacterial assays presented in table 6.

Conclusion

In conclusion, this study successfully synthesized and characterized a novel macrocyclic ligand and its metal complexes using a combination of analytical techniques including ^{1}H-NMR, ^{13}C-NMR, UV-Vis, FT-IR, elemental analysis and atomic absorption spectroscopy. These analyses confirmed the mononuclear structure of the metal complexes.

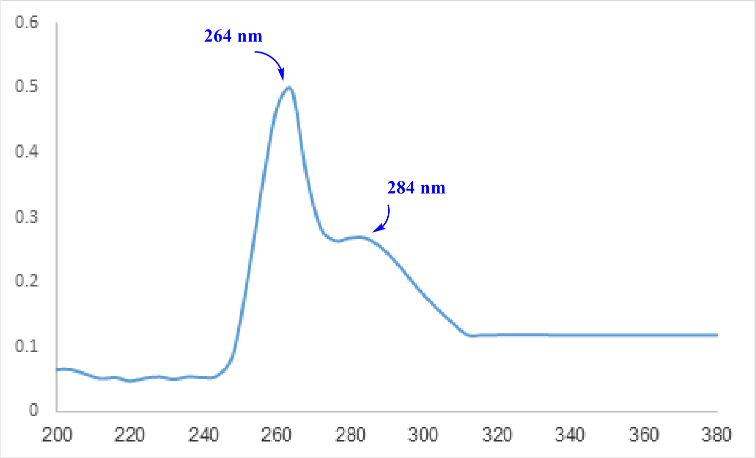

Fig. 18: UV-VIS spectrum of [Zn (TMADEH)(H_2O)$_2$]Cl_2

Table 3
The electronic transitions for TMADEH and their complexes

Comp.	**$\pi \rightarrow \pi*$**	**$n \rightarrow \pi*$**	**d-d**
TMADEH	264 nm	296 nm	------
[Co (TMADEH)Cl_2]	264 nm	284 nm	535,615,685
[Cu (TMADEH)(H_2O)$_2$]Cl_2	264 nm	288 nm	904
[Zn (TMADEH)(H_2O)$_2$]Cl_2	264 nm	284 nm	-----

Table 4
The Elemental analysis for TMADEH

$C_{12}H_{24}N_8$		**Comp.**
Found %	**Calculated %**	
49.32	51.40	C
8.11	8.62	H
38.01	39.9	N

Table 5
The Atomic absorption spectroscopy for complexes

Comp.	**Calculated %**	**Found %**
[Co (TMADEH)Cl_2]	14.36	13.99
[Cu (TMADEH)(H_2O)$_2$]Cl_2	14.676	13.879
[Zn (TMADEH)(H_2O)$_2$]Cl_2	14.45	12.86

Table 6
Biological test results of the P. aeruginosa and S. aureus

Entry	50 (µg/mL)		100 (µg/mL)	
	Staphylococcus aureus **(+)**	***Pseudomonas aeruginosa*** **(-)**	***Staphylococcus aureus*** **(+)**	***Pseudomonas aeruginosa*** **(-)**
Gentamicine	23	23	27	24
DMSO	0	0	0	0
TMADEH	8	14	13	16
[Cu (TMADEH)$(H_2O)_2$]Cl_2	14	11	15	14

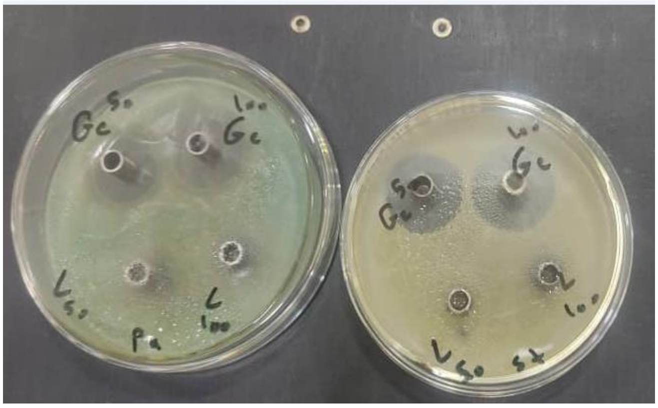

Fig. 19: Inhibition zone at different concentration against Gram-positive and Gram–negative to (TMADEH)

Fig. 20: Inhibition zone at different concentration against Gram-positive and Gram–negative to [Cu (TMADEH]Cl_2.$2H_2O$

Furthermore, the biological activity of the synthesized compounds against *Pseudomonas aeruginosa* and *Staphylococcus aureus* bacteria was investigated. The results revealed that the prepared metal complexes exhibited greater biological activity compared to the Schiff base ligands. This finding holds promise for the potential use of these compounds in various pharmacological applications indicating their potential for further development and exploration in the field.

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