STM JOURNALS

Journal of
Polymer & Composites

https://journals.stmjournals.com/JOPC/

ISSN: 2321-2810 (Online)
ISSN: 2321-8525 (Print)
Volume 12, Special, Issue 6, 2024
DOI (Journal): 10.37591/JoPC

Research JoPC

Recent Advances in Transition Metal Complexes with Phenyl Acetic Acid and Pseudo Halogen: Synthesis, Characterization and Applications

AK. Sanivarapu[1,*], BK Babu[2], D. Sravani[3], U. Naga Babu[4], SK Raziya[5]

Abstract

A well-established strategy is to introduce a biologically relevant organic molecule in coordination sphere of transition metal complexes to increase the selectivity and biocompatibility. Phenylacetic acid (PAA), an organic molecule with a phenyl functional group and a carboxylic acid functional group, is a phenylalanine that is generated from the naturally occurring auxin, which is extensively present in plants. The most promising outcomes in the battle against cancer and microbes come from metal complexes having ligands including bio molecules. In this work we synthesized two complexes of copper with phenyl acetic acid as primary ligand and pseudo halide and orthophenyl diamine as secondary ligands and characterized them by IR, LC-MS, UV and TG-DTA. Later investigated for antimicrobial and cytotoxic activity. The results indicate that these complexes of phenyl acetic acid have proved that they are good antibacterial agents in comparison with the cytotoxicity against MCF-7, A-431, HepG-2. The complex1 which is having pseudo halide as secondary ligand is found to have good battle against cancer and microbes than the other complex2 which is having orthophenyl diamine as secondary ligand. This is because pseudo halides have ability to disrupt cell membranes, enzymes or metabolic process in microorganisms.

Keywords: Phenylacetic acid, biocompatibility, biomolecules, metal complexes, ligand

***Author for Correspondence**
AK. Sanivarapu
E-mail: arunasanivarapu189@gmail.com

[1]Associate Professor, Department of Chemistry, Aditya University, Suramplaem, Andhra Pradesh, India
[2]Associate Professor, Department of Engineering Chemistry, AU College of Engineering, Visakhapatnam, Andhra Pradesh, India
[3]Associate Professor, Department of Chemistry, Aditya College of Engineering and Technology Suramplaem, Andhra Pradesh, India
[4]Associate Professor, Department of Engineering Chemistry, SRKR College, Bhimavaram, Andhra Pradesh, India
[5]Assistant Professor, Department of Basic Sciences & Humanities, Viskha Institute of Engineering & Technology, Narava, Viskhapatnam, Andhra Pradesh, India

Received Date: April 24, 2024
Accepted Date: June 25, 2024
Published Date: September 23, 2024

Citation: AK. Sanivarapu, BK Babu, D. Sravani, U. Naga Babu, SK Raziya. Recent Advances in Transition Metal Complexes with Phenyl Acetic Acid and Pseudo Halogen: Synthesis, Characterization and Applications. Journal of Polymer & Composites. 2024; 12(6): S68–S78p.

INTRODUCTION

Transition elements have structural and functional roles in numerous biological processes, including electron transport, catalysis, and enzyme and protein active sites [1]. However, abnormal metabolic processing of certain of these important metals has been linked to the emergence of numerous clinical conditions, including cancer [2]. A number of metal-based compounds have been created that exhibit potential anticancer effects; some of these compounds are now undergoing clinical trials, while others are already being used in clinical practice for cancer detection and therapy. Recently created metal-based compounds have a different range of cytotoxicity [3, 4] and are the result of drug design aimed at attaining certain goals that the original chemical was unable to accomplish. Different biological actions are displayed by transition metals [5] on chelating to a metal may have a stronger antimicrobial impact [6] and copper complexes, for instance, exhibit remarkable antibacterial action [7].

In 19th century itself Auxins are identified as class of hormone which has a role in almost every area of plant life. Indole-3-acetic acid (IAA) is the first phyto hormone and another is phenyl acetic acid (PAA). Phenyl acetic acid is a chemical that stimulates growth in plant [8–12]. Phenyl acetic acid is used in several industries like textile, plastic, paper, insecticides, pesticides, cosmetics and also used in the synthesis of penicillin. It is also having antibacterial activity [13]. From previous papers orthophenyl diamine is found be a potent anti-cancer agent against breast cancer, osteosarcoma, lymphoma and melanoma cells [14]. As pseudohalides like Thiocyanate and azide bridge metal centers providing complexes with fascinating physical properties we have selected them as secondary ligand [15–20]. We have synthesized several metal complexes with several biological active ligands and two such complexes are copper complexes using phenyl acetic acid as primary ligand and pseudo halide (Thiocyanate) and orthophenyl diamine as secondary ligand [21–25].

EXPERIMENTAL MATERIALS AND METHODS

Synthesis of metal complex 1&2

A solution of $Cu(ClO_4)_2 \cdot 6H_2O$(0.5mM) is added upto PAA(phenyl acetic acid)(0.5mM) and NaOCN (sodium thiocyanate)(1mM) under stirring conditions at 60°C for 30 minutes. The precipitate which is formed is washed with a solution of methanol.

A solution of $Cu(ClO_4)_2 \cdot 6H_2O$(0.5mM) is added upto PAA(phenyl acetic acid) (0.5mM) and $C_6H_4(NH_2)_2$ (ortho phenyl diamine) (1mM) under stirring conditions at 60°C for 30 minutes. The precipitate which is formed is washed with a solution of methanol.

RESULTS AND DISCUSSION

The results obtained from the synthesis of metal complex 1 and 2 which are obtained are characterized with help of UV, IR spectroscopy and LC-MS Spectroscopy

IR spectrum of Metal Complex 1

In the complex band is caused due to ν (O-H) at3420 cm^{-1}caused due to ν(NCO) at 2259 cm^{-1} (Figure 1).

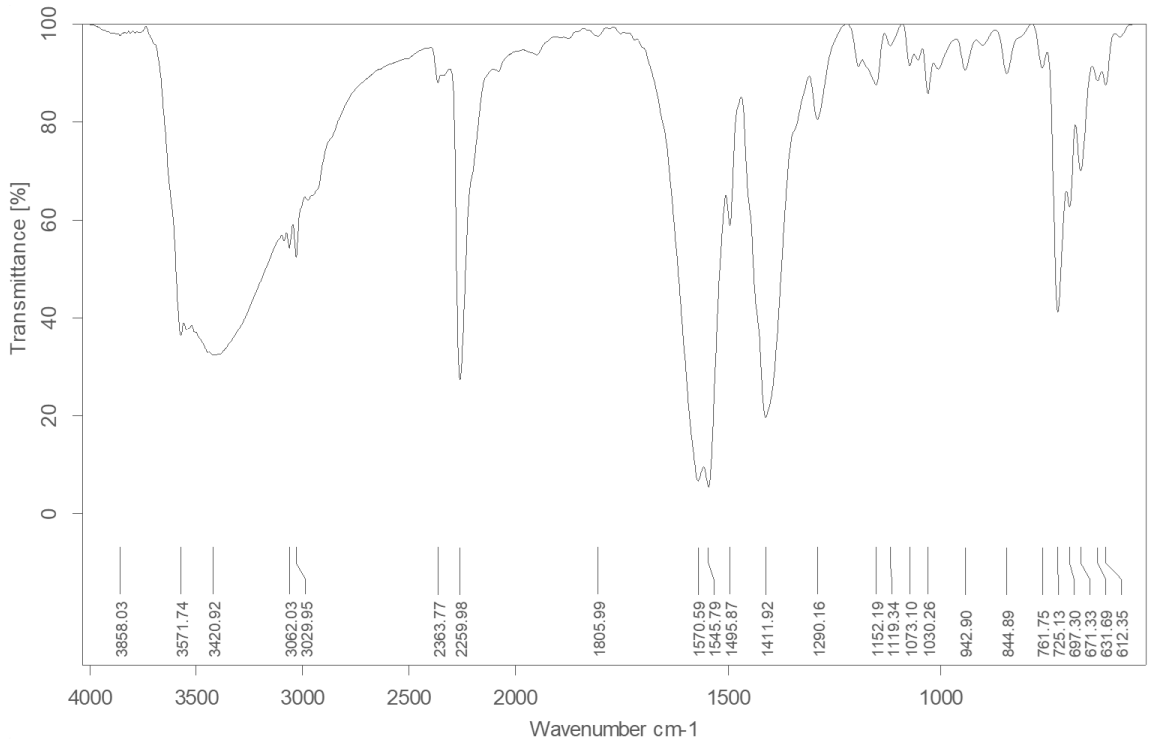

Figure 1. IR Spectra of Metal Complex 1.

IR Spectra of Metal Complex 2

In the complex band is caused due to ν(O-H) at 3383cm^{-1}, due tov (C=N)at 1514cm^{-1} and at 1087 is due to ν (ClO_4) (Figure 2).

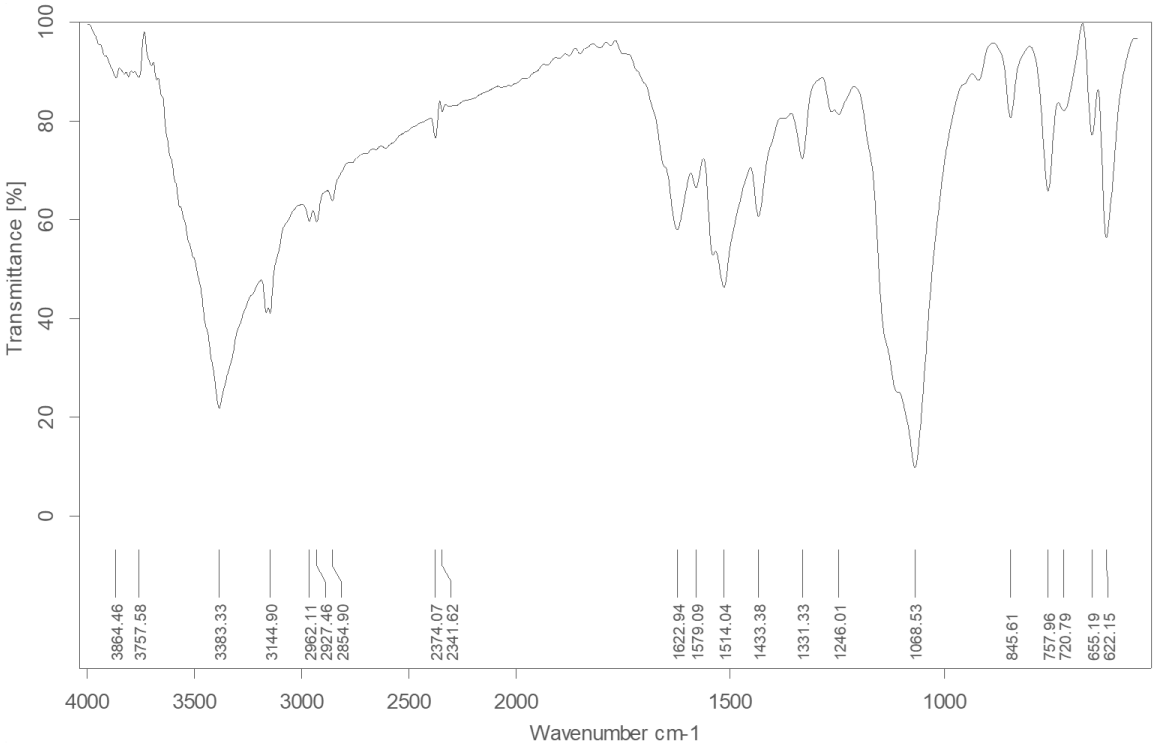

Figure 2. IR Spectra of Metal Complex 2.

Mass Spectra of Metal Complex 1

The Mass Spectra of Metal Complex 1 showed peaks at various placespeak at 380(m/z) agree with the complex [Cu(PAA)$_2$(NCO)], at 425(m/z) agree with the complex [Cu (PAA)$_2$(NCO)$_2$] and at 447(m/z) agree with the complex [Cu (PAA)$_2$(NCO)$_2$.H_2O] (Figure 3).

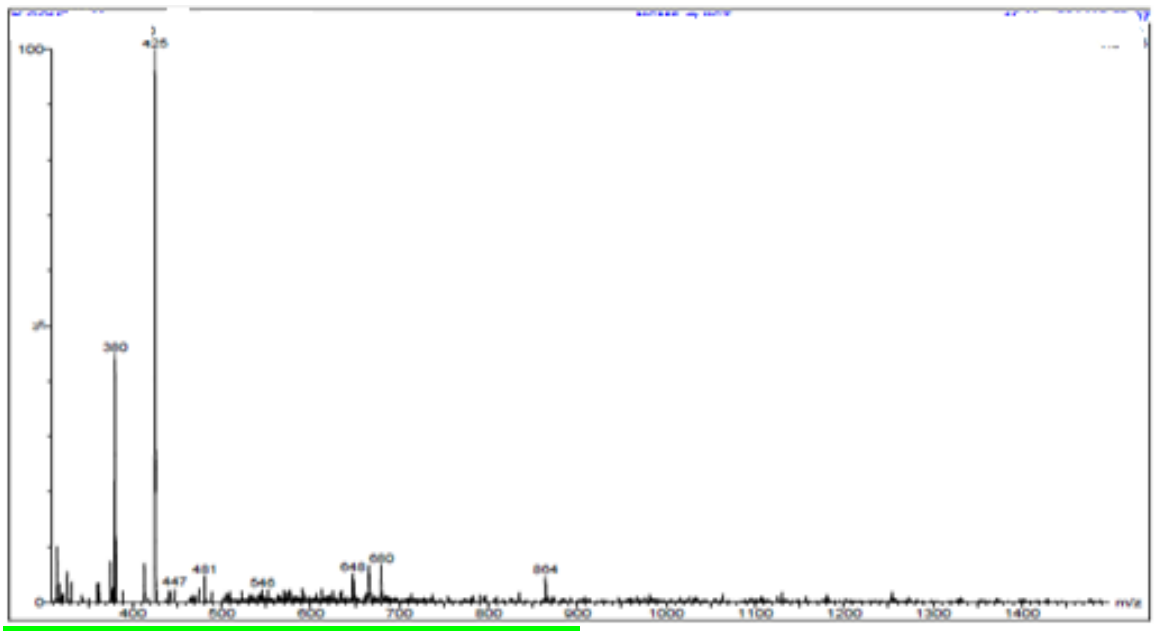

Figure 3. LC-MS Spectra of Metal Complex (1).

Mass Spectra of Metal Complex 2

The Mass Spectra of Metal Complex 2 showed peaks at various places the peak at 169(m/z) agree with the complex [Cu(OPD)] and at 648 (m/z) agree with the complex $[Cu(PAA)_2(OPD)(ClO_4)_2]$ (Figure 4).

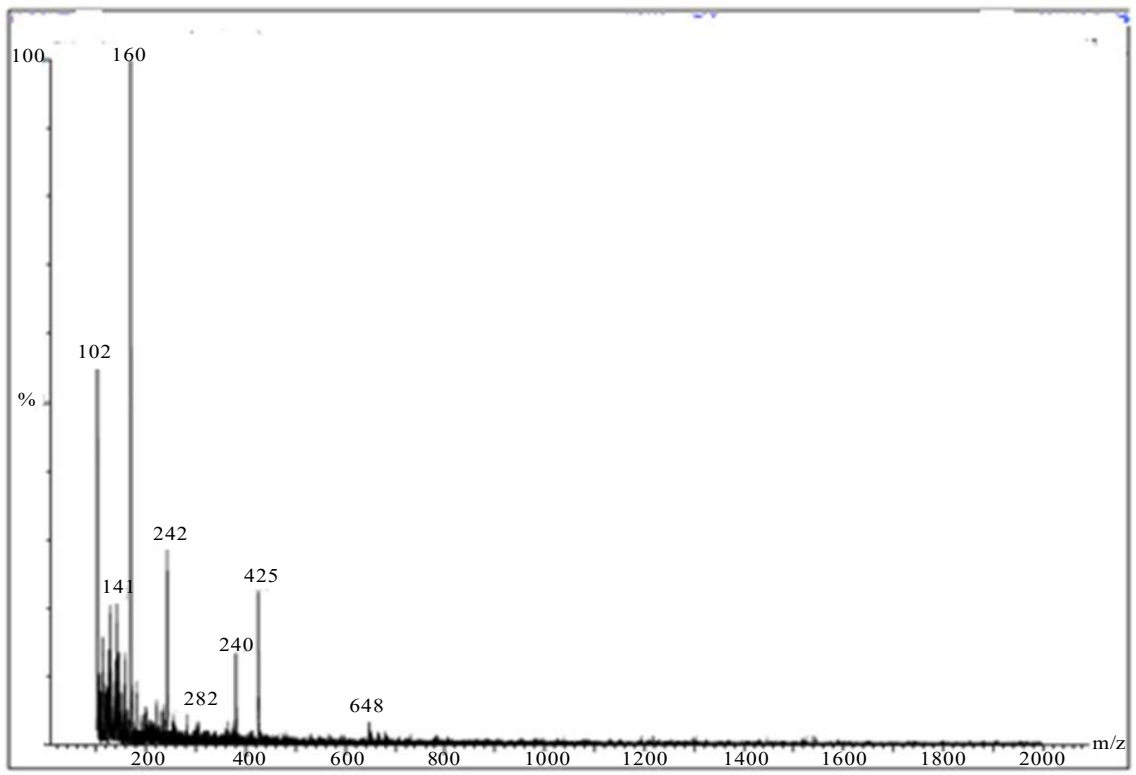

Figure 4. LC-MS Spectra of Metal Complex (2).

UV-Visible spectra of metal Complex 1

In DMSO as solvent the UV-VISIBLE spectrum of the metal complex 1 is reported as the wavelength range 200–800nm using DMSO as solvent which showed a broad band at 360 nm (Figure 5).

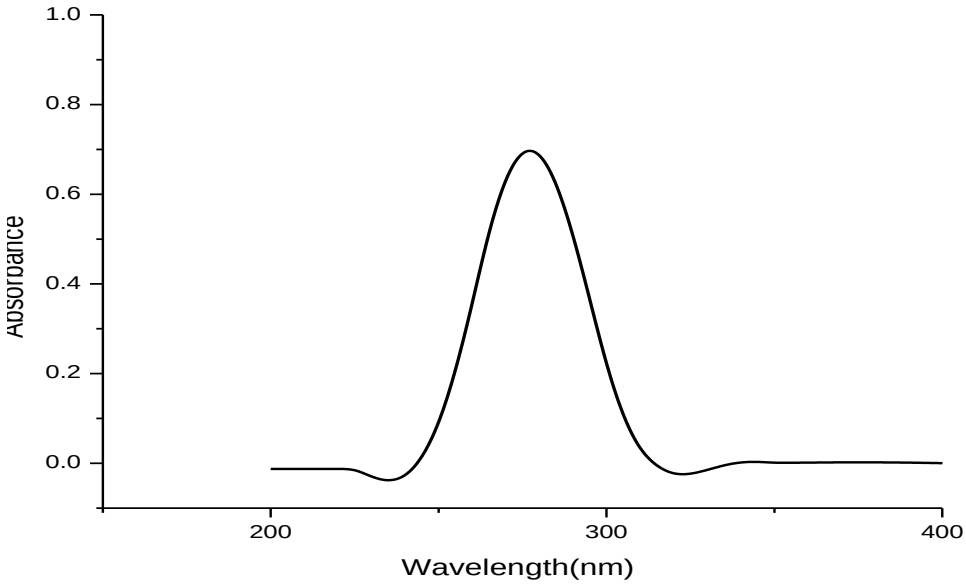

Figure 5. Electronic Spectrum of Complex (1).

UV-Visible Spectra of Complex 2

In DMSO solution, the metal complex UV-VISIBLE spectrum is recorded between 200 and 800 nm which showed a band at 280nm and 360nm (Figure 6).

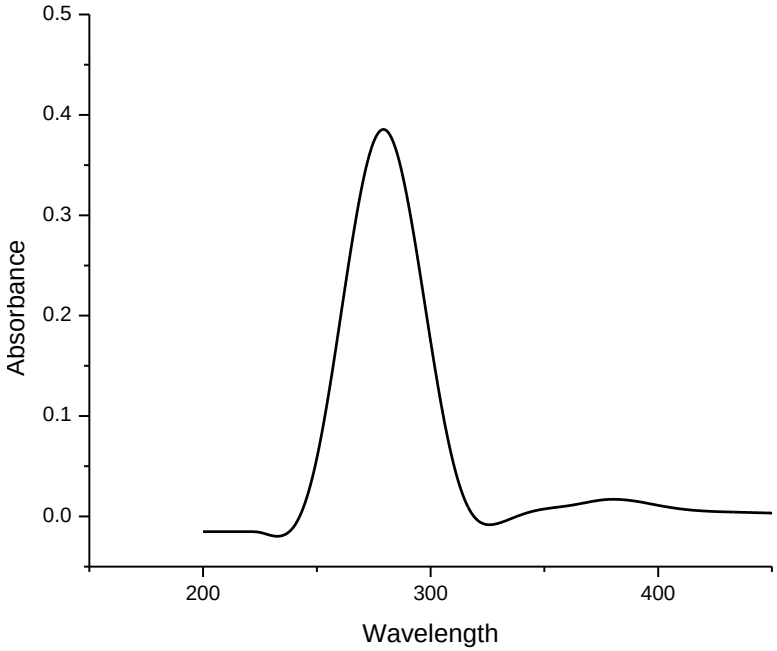

Figure 6. Electronic Spectrum of Metal Complex (2).

TG-DTA Spectra of MetalComplex 1

The thermal decay of the Metal complex 1takes place at 50-200°C with loss in mass about 11.5% (obs 11.7%)which is in accordance with DTA peak at 100°C. Loss of PAA occurs at 200-300°C in accordance with DTA peak observed at 220°C.Third stage is loss of PAA & NCO between 300-500°Cwith loss in mass loss is 45.6%(obs 46.6%).The data of the spectrum are represented in the Figures 7 and 8.

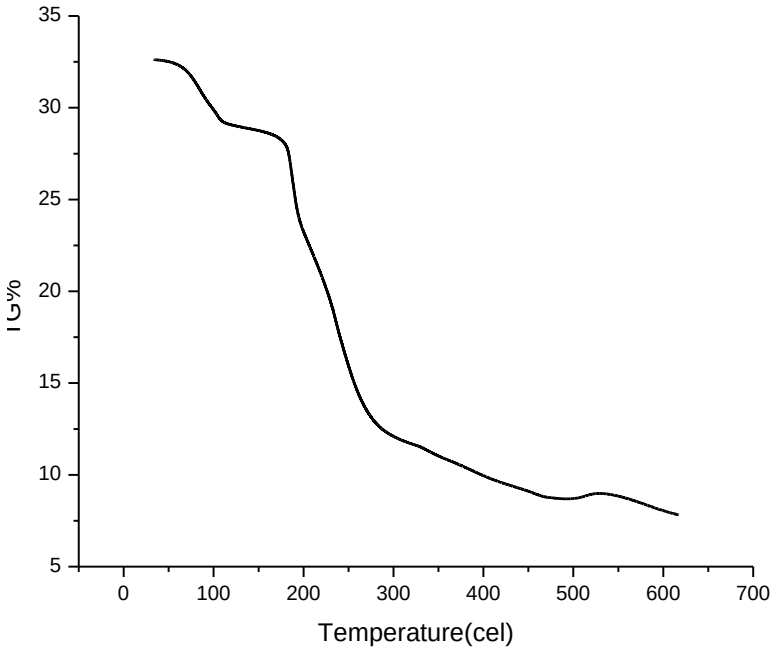

Figure 7. TG Spectra of Metal complex (1).

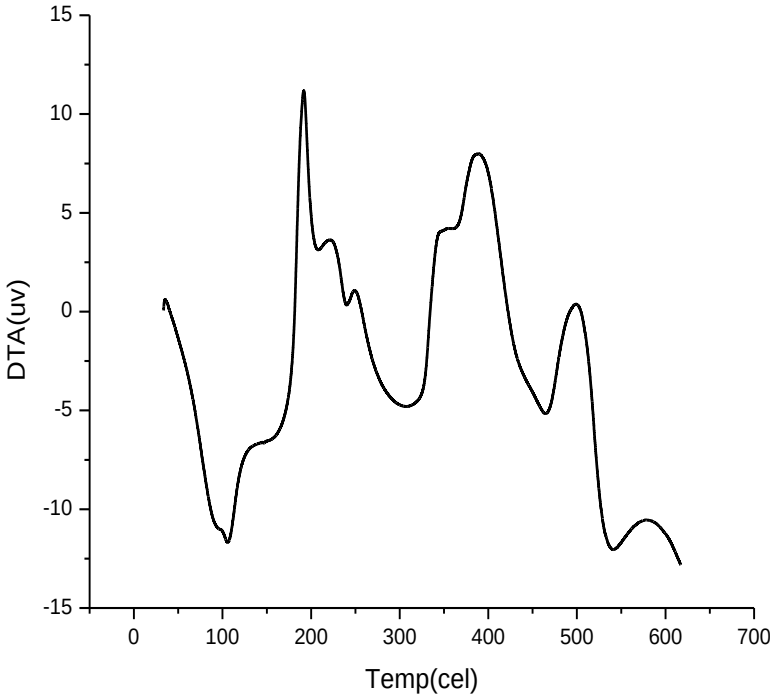

Figure 8. DTA Spectrum of Metal Complex (1).

TG-DTA spectra of Metal Complex 2

The decay studies of metal complex 2 takes place at200-250°Cwith mass loss of 14.2%(Obs14.6%) which is in accordance with DTA peak observed at 220°C.In the second stage decomposition of PAA and OPD ligand takes place in between 250-400°C which is in accordance with DTA peak observed at 250°C with mass loss of 64.2% (obs 67.8%). The data of the spectrum are represented in the Figures 9 and 10.

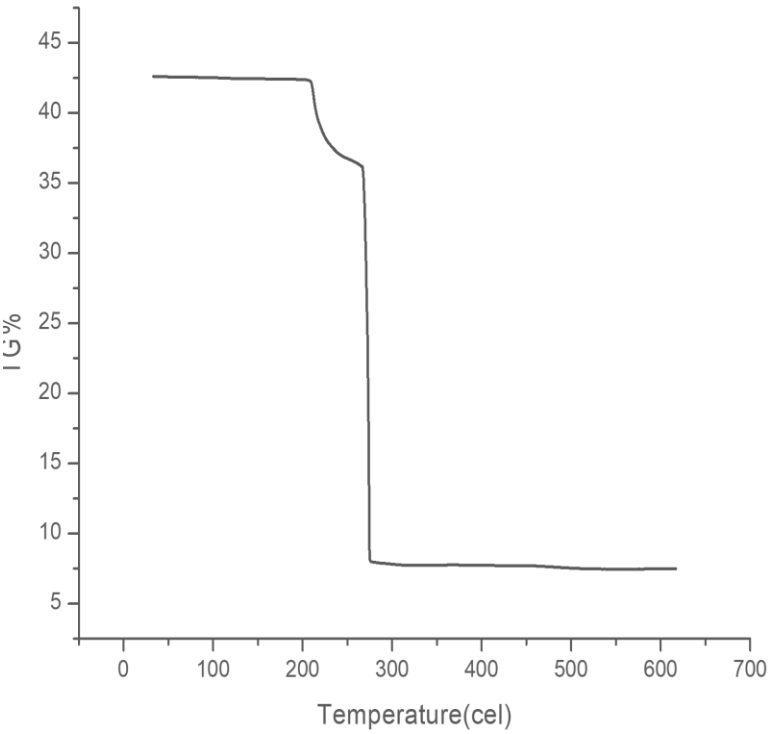

Figure 9. TG Spectrum of Metal complex (2).

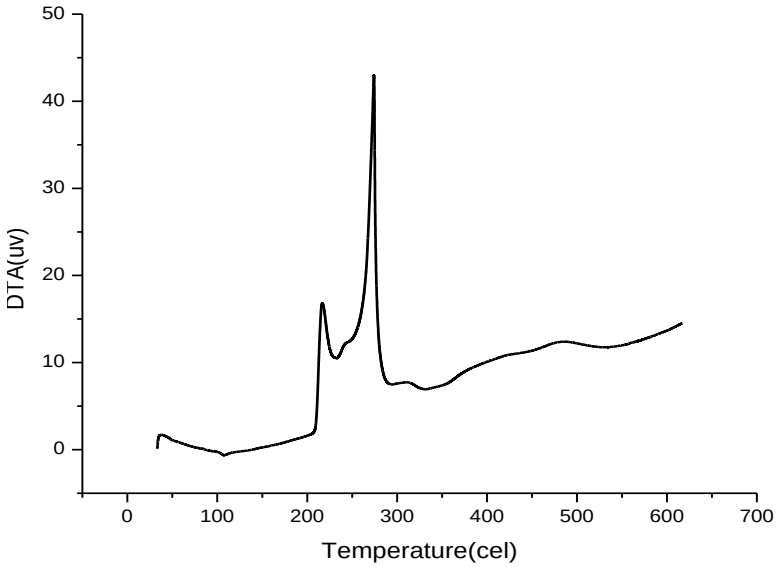

Figure 10. DTA Spectrum of Metal Complex (2).

Antimicrobial Screening of Metal Complex 1

The antimicrobial activity metal complex 1 is examined by disc diffusion method for (*E.coli, S.aureus, P.aeruginosa and against R.Oligospores)*(Tables 1-2).

Table 1. Zone of Inhibition in metal complex 1.

S.N.	Microorganism	Zone of inhibition
1	*P.aeruginosa*	3.5 mm
2	*S.aureus*	9 mm
3	*E.coli*	10 mm
4	*R.Oligospores*	Nil

Figure 11. Zone of inhibition against *S.aureus*

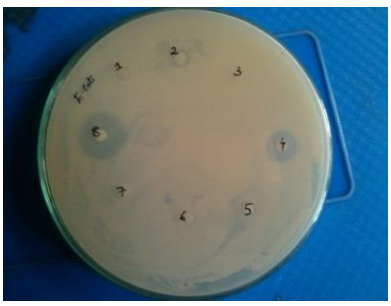

Figure 12. Zone of inhibition against *E.coli*

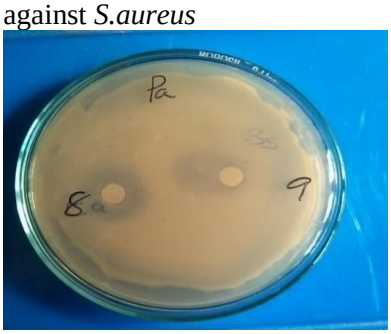

Figure 13. Zone of inhibition against *P.aeruginosa*

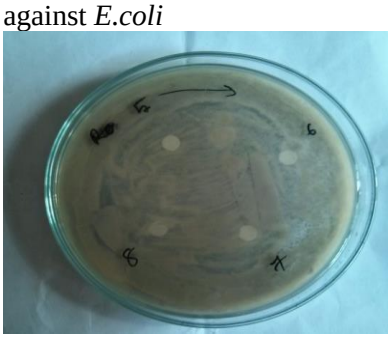

Figure 14. Zone of inhibition against *R.Oligospores*

The following images represent the zone inhibition exhibited by the bacteria and fungi S.aureus, E.coli, *P.aeruginosa*, R.*Oligospores* in the Figures 11 to 18.

Table 2. Zone of inhibition exhibited by metal complex 2.

S.N.	Microorganism	Zone of inhibition
1.	*S.aureus*	5 mm
2.	*E.coli*	3 mm
3.	*R.Oligospores*	Nil

Cytotoxicity Studies of Metal Complex 1

Cytotoxicity of metal complex 1 screened for cell lines like Breast (MCF-7), Epidermoid (A-431) cancer cell lines. The values are represented in Tables 3 and 4.

a. Cytotoxic activity of metal complex 1 for breast cell line

Table 3. Cytotoxicity of metal complex 1 on Breast (MCF-7) cancer cell line.
Growth period: 24 hour

Conc(µg/ml)	OD of extract	% Cell Survival	%Cell inhibition
	0.694	100	0
0.1	0.5785	83.35	16.65
1	0.56	80.69	19.31
10	0.5475	78.89	21.11
100	0.2455	35.37	64.63
500	0.1	14.4	85.6

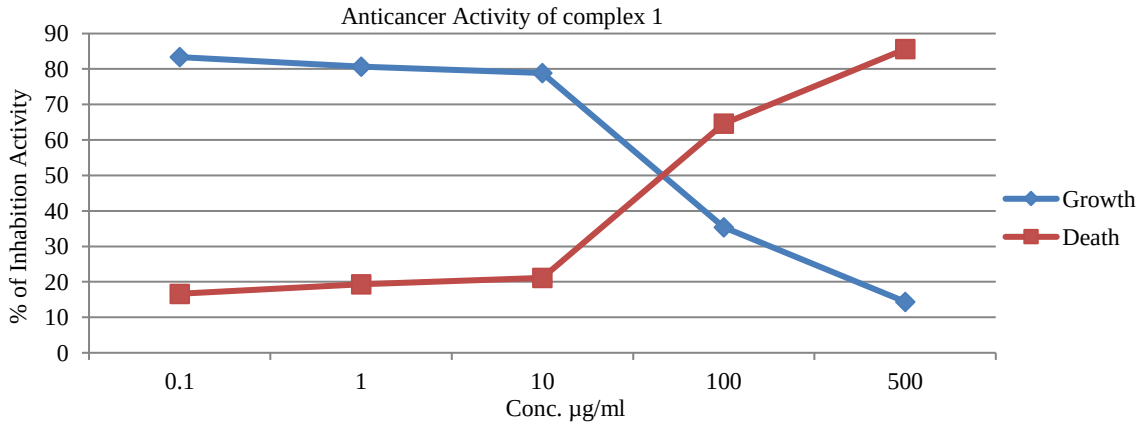

Figure 15. Effect of metal complex 1 on Breast (MCF-7) Cell line.

IC_{50}	69.0 µg/ml

a. Cytotoxicity of metal complex 1 on epidermiod cell

Table 4. Cytotoxicity of metal complex 1 on Epidermoid (A-431) Cell line.

Conc(µg/ml)	OD of extract	%Cell Survival	%Cell inhibition
	0.994	100	0
0.1	0.938	94.36	5.64
1	0.913	91.85	8.15
10	0.8715	87.67	12.33
100	0.4083	41.07	58.93
500	0.195	19.61	80.39

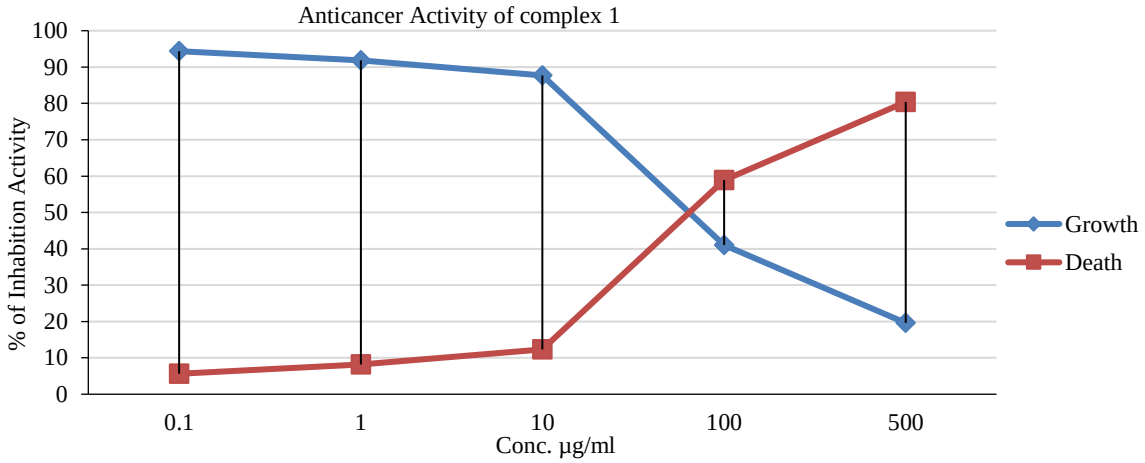

Figure 16. Effect of complex 1 on Epidermoid (A-431) Cell line.

IC_{50}	**82.18 µg/ml**

Cytotoxic Studies of Metal Complex 2

Cytotoxicity of complex 2 screened for cell lines like Breast (MCF-7) and Epidermoid (A-431) cancer cell lines(Table 5).

a. Cytotoxic active ity of metal complex 2 for breast cell line

Table 5. Cytotoxicity of complex 2 on Breast (MCF-7) Cell line.
Growth period: 24 hours

Conc (µg/ml)	OD ofextract	%Cell survival	%Cell inhibition
	0.694	100	0
0.1	0.601	86.59	13.41
1	0.583	84	16
10	0.536	77.23	22.77
100	0.398	57.34	42.66
500	0.198	28.53	71.47

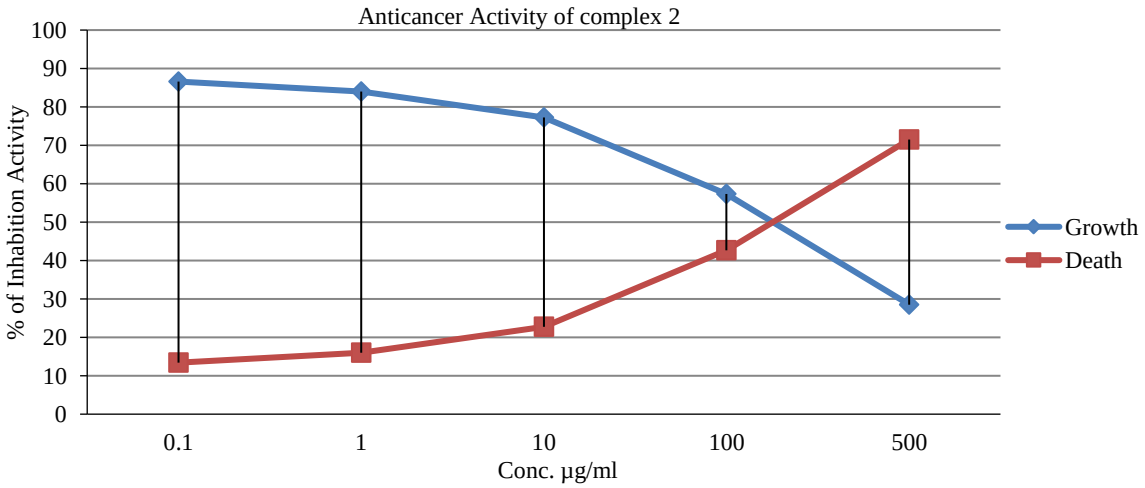

Figure 17. Effect of complex 2 on Breast (MCF-7) Cell line.

IC_{50}	**201.92 µg/ml**

a. Cytotoxicity of complex 2 on epidermiod cell

Table 7. Cytotoxicity of complex 2 on Epidermoid(A-431) Cell line.
Growth period 24 hours

Conc(µg/ml)	OD of extract	% Cell Survival	% Cell Inhibition
0.1	1.018	100	0
1	0.978	96.07	3.93
10	0.975	95.77	4.23
100	0.645	63.35	36.65
500	0.618	60.7	39.3

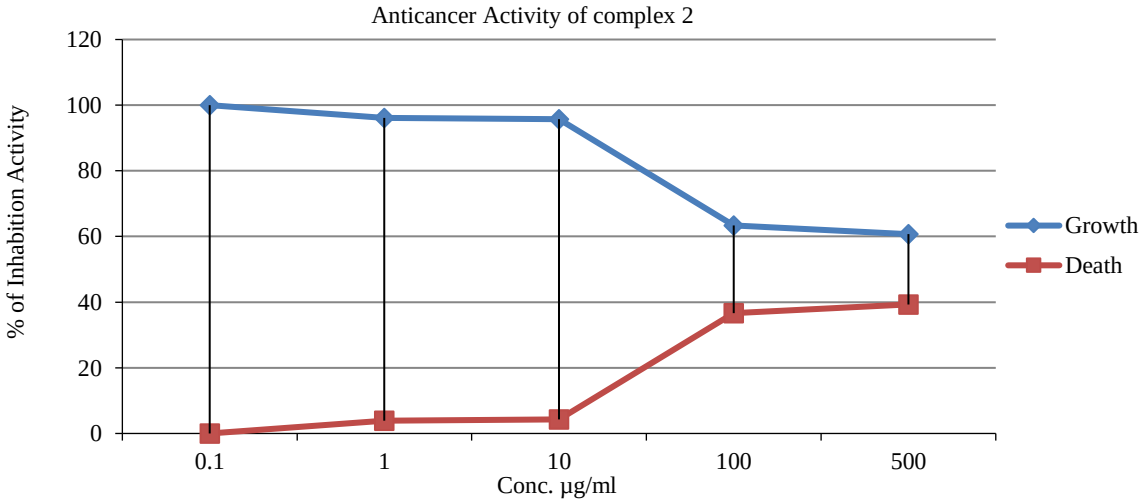

Figure 18. Effect of complex 2 on Epidermoid (A-431) Cell line.

IC_{50}	236.98 µg/ml

CONCLUSION

The novel mixed ligand complexes were successfully synthesized by taking Cu (II) and primary ligand as Phenyl acetic acid and secondary ligands such as iso-cyanate and ortho phenyl diamine. These complexes are well characterized by using FT-IR, LC-MS, UV-VIS, and TG-DTA. Furthermore, the mixed ligand complexes were screened invitro for antibacterial activity against bacteria such as*P.aeruginosa*, *E.Coli*, *S.aureus* and fungus such as *R.oligospores*. Further these complexes are also screened for cytotoxicity against the cell lines MCF-7, A-431, HepG-2. As phenyl acetic acid is having good antimicrobial activity these complexes are having good antibacterial activity then the antifungal activity. Hence these complexes of phenyl acetic acid have proved that they are good antibacterial agents in comparison with the cytotoxicityagainst MCF-7, A-431, HepG-2.We have found that the complex1 which is having pseudohalide as secondary ligand is found to have good battle against cancer and microbes than the other complex2 which is having orthophenyldiamine as secondary ligand. This is because pseudohalides have ability to disrupt cell membranes, enzymes or metabolic process in microorganisms. Hence it might be a suitable strategy to develop novel therapeutic on further studies.

REFERENCES

1. Orvig C, Abrams MJ. *Medicinal inorganic chemistry: introduction. Chem Rev*.1999; 99:2201–4p.
2. Yaman M, Kaya G, Yekeler H. Distribution of trace metal concentrations in paired cancerous and non-cancerous human stomach tissues. *World J Gastroenterol*.2007;13:612–8p.
3. Palma G, D'Aiuto M, Rea D, et al. Organo-metallic compounds: novel molecules in cancer therapy. *Biochem Pharmacol Open Access*. 2014 ;13(13):1603–1615p.

4. Santini C, Pellei M, Gandin V, et al. Advances in copper complexes as anticancer agents. *Chem Rev*. 2014; 114(1):815–862p.
5. AngT'.A, Lien E.J. *J. Clin. Pharm. Ther*.1981; 6,45 p.
6. Braicu C, Stanila A, Rotar A, et al. *USAMV Agric*.2006; 62: 207p.
7. Faúndez G, Troncoso M, Navarrete P, et al. *BMC Microbiol*. 2004; 4:19p.
8. Eriksen S.H, Bengt Søderblom.T, Jensen.B. *Biotechnol. Bioeng*. 1998; 60:310p.
9. Lee J.G, Lee B.Y, Lee.H.J. *Sci. Hortic*. 2006; 110: 119p.
10. Pizzeghello D, Zanella A, Carletti P et al. *Chemosphere.* 2006; 65:190p.
11. Burkhead k.D, Slininger P.J,Schisler.D.A. *Soil Biol. Biochem*. 1998; 30:665p.
12. Zhu Y.J, Zhou H.T, Hu Y.H et al. Liu. *Food Chem*.2011, 124:298p.
13. Sheu C.W, Salomon.D, Simmons.J.L et al. *Antimicrob. Agents Chemother*.1975; **7:** 349p.
14. Lida J, Bell-Loncella E.T, Purazo, M.L, et al. Inhibition of cancer cell growth by ruthenium complexes, *J Transl Med*. 2016, 14: 48p.
15. Mohamed M. El-bendary, Muhammad N, et al Structure characterization and antitumor activity of palladium pseudo halide complexes with 4-acetylpyridine, *Journal of Coordination Chemistry*.2019, 72(18),3088–3101p.
16. Ribas J, Escuer.A, Monfort.M, et al. *Coord Chem.Rev*.1999,1027:193p.
17. Robin R, Abrahms B.F, Barten R.R, et al .Supramolecular Architecture, American *Chemical Society, Washington,DC,*1992.
18. Mautner F.A, Fischer R.C, Reichmann K ,et al. *J.Mol.Struct*. 2019, 1175:797p.
19. Ruiz.E, Cano.J, Alvarez.S, et al .*J.Am.Chem.Soc*. 1998,120: 11122p.
20. Etaiw S.E.H,El-Bendary M.M ,Fouda.S.S et al. Prot.Met.*Phys.Chem.Surf*; 2017,53:937.
21. ArunaKumari S, Kishore Babu B, China satyanarayana Ch, et al. Metallopharmaceuticals : synthesis,characterization and bio-active studies, *Indian Journal of Biochemistry & Biophysics*,2019,56.
22. ArunaKumari S, Kishore Babu B, Prasad M.S.N.A et al . Bio-Active Phenylacetic Acid Complexes : Synthesis, Structure And Antimicrobial Activities, *Journal of Chemical and Pharmaceutical Sciences*,2019,12(1),10–13p.
23. ArunaKumari S, Kishore Babu B, Mohanarao K et al. Bio-Active Amino Acid Complexes : Synthesis, Structure And Antimicrobial Activities, *Journal of Chemical and Pharmaceutical Science.*2019,12(2),47–50p.
24. Sanivarapu AK, Babu BK, Anil Kumar B et al. Anti pathogenic studies of new mixed ligand metal chelates, *Indian Journal of Biochemistry & Biophysics* .2022,59:189–196p.
25. Aruna Kumari S ,Aruna P, Babu BK, et al. Cytotoxic and microbial studies of mixed metal complexes, *Indian Journal of Biochemistry & Biophysics* . 2023, 60 : 231–236p.

