

## **Synthesis, Characterization, antimicrobial and Cytotoxic Studies on transition metal complexes of pentamethylene dithiocarbamate and diamines**

D.Malathy, R.Vijayanthimala\*

*Department of Chemistry, Ethiraj College for Women, Chennai-8, Tamil nadu, India*

---

**Abstract:** A new series of Ni(II), Zn(II) and Cu(II) mixed ligand complexes of pentamethylenedithiocarbamate (pmdtc) with diamines such as ethylene diamine (en), diethylenetriamine (dien) and triethylenetetramine (trien) are reported. The synthesized complexes were characterized by elemental, thermal and magnetic analysis, UV-Visible, infra-red, Nuclear Magnetic Resonance and ESR Spectral studies. Antibacterial, antifungal, anticancer activities have also been carried out for these complexes. All the complexes have shown reasonable activity indicating a promising future for the mixed ligand complexes of Ni (II), Zn (II), and Cu (II) in biological field with less side effects.

**Keywords:** Ni (II), Zn (II), Cu (II), pentamethylene dithiocarbamate, en/dien/trien, antibacterial antifungal anticancer

---

### **I. Introduction**

Disease causing microbes that have become resistant to drug therapy are an increasing public health problem. Responding effectively to these bacterial infections requires rational use of drugs especially the ones which are the last line of defence, by understanding the mode of resistance and equipping ourselves with newer and advanced antibiotics by discovering new antibiotics or developing the antibiotics already in use, making them more active. Therefore there is an urgent need to develop new bactericides. Various antimicrobial agents have been developed for curing and preventing diseases in public health hygiene and antifouling in biomedical industry. One aspect of drug discovery focusses on the modification of the structure of existing drug, resulting in a change in potency and selectivity with little side effects/ low toxicity. In this connection, ligands coordinating through sulfur atoms, especially dithiocarbamates are deserving much attention in recent years, and a large number of dithiocarbamate complexes with transition metals have been synthesized and investigated for anticancer, antiviral, antifungal, antibacterial, myocardial tracer and AIDS therapy [1-14]. The incorporation of transition metal in to dithiocarbamate ligands have shown to possess increased biological activity and also it has found that antimicrobial activity highly depends on the nature of ligands present [15,16]. The present study describes the synthesis, characterization, antimicrobial and anticancer activities of Ni(II), Zn(II) and Cu(II) mixed ligand complexes of pentamethylenedithiocarbamate with diamines.

### **II. Experimental Section**

**2.1 Materials:** The chemicals employed for the preparation are of very pure grade and used without further purification. The Nickel chloride, Zinc sulphate and Copper chloride used for the synthesis are of analytical grade. Piperidine, carbondisulphide, Ethylenediamine, diethylenetriamine, triethylenetetraamine are pure grade chemicals from Merck. The chloroform used as solvent in all our studies is distilled by standard procedures. The Metal present in the complex was estimated using ICP-OES (Inductively Coupled Plasma optical emission spectroscopy- PerkinElmer Optima 5300 spectrometer). The nitrogen and sulphur were estimated by Kjeldhal's method and barium sulphate method respectively. TGA/DSC were recorded in nitrogen atmosphere using NETZSCH STA 490C/CD thermal analyser with a heating rate of 10°/min. Magnetic susceptibility studies were carried out using Vibrating sample magnetometer Lakeshore VSM 7410. UV-Visible absorption spectra (in chloroform) were recorded using a Shimadzu UV 1600 model spectrometer. The IR spectrum of the complexes were recorded as KBr disc using Shimadzu Spectrometer. The EPR spectra of the complexes were recorded using JES-FA200 EPR spectrometer in the region from 1000-8000 gauss. Proton NMR spectrum for the diamagnetic complexes were recorded using Bruker AVANCE III 500 MHz (AV 500) multi nuclei solution NMR Spectrometer. The bactericidal and fungicidal activities of the complexes were studied by agar disc diffusion method originally described by Baur [17]. The invitro cytotoxicity of the prepared complexes were carried out by MTT based assay [18] with cancer cell line, MCF-7 (human breast cell line). In parallel the activity was tested on normal cell line, VERO (monkey kidney cell line).

**2.2 Preparation Ni (II), Cu (II) and Zn (II) Dithiocarbamate Complexes:**

[M (pmdtc)<sub>2</sub>(diamine)]

The preparation of the complexes were done as per the literature reported by us [19]. The preparation follows two step synthesis wherein the dithiocarbamate is generated first and then the mixture containing the metal, to which diamine is added, is then made to react with the dithiocarbamate resulting in the formation of mixed ligand complexes. The insoluble complexes precipitate and are filtered. The complexes repeatedly washed with alcohol and water mixture and recrystallised from ether and dried in vacuum.

### III. Results and discussion

The complexes are stable, non-hygroscopic and colored solids except zinc. All the complexes were found to be completely soluble in chloroform and DMSO, partially soluble in DMF and insoluble in alcohol and water. The elemental analysis data of the complexes (Table-1) confirm the proposed composition [M (pmdtc)<sub>2</sub>(diamine)]. The electrical molar conductance of the complexes at a concentration of about 10<sup>-3</sup> M in chloroform solution was found to be 5-10 Ohm<sup>-1</sup> cm<sup>2</sup>mol<sup>-1</sup> indicating the non-electrolytic nature of the complexes [20]. The thermal analysis data from TGA for the complexes are furnished in table-1. The thermograms were run upto 1000° C and final residue corresponded to metal sulphide. The IR spectral data of the complexes are given in Table-2. The stretching vibration of νNH of amines appears around 3420cm<sup>-1</sup>. The aliphatic C-H of amine appears around 2860 cm<sup>-1</sup> and ν C-H of piperidine appears around 2930 cm<sup>-1</sup>. The νC=S stretching frequency appears around 1230 cm<sup>-1</sup>. The two bands around 870-1010cm<sup>-1</sup> are assigned to ν C-S group of dithiocarbamate moiety and these confirms bidentate and monoionic nature of dithiocarbamate[21]. The bands in the region 1250-1350cm<sup>-1</sup> are assigned to ν N-C stretching vibration. The electronic spectral data of the complexes in chloroform were recorded and the results are given in Table-1. The Ni(II) complexes show three bands around 630-653, 380-400 and 420-460 nm which corresponds to three spin allowed transitions <sup>3</sup>A<sub>2g</sub>→<sup>3</sup>T<sub>2g</sub>, <sup>3</sup>A<sub>2g</sub>→<sup>3</sup>T<sub>1g</sub>(F), <sup>3</sup>A<sub>2g</sub>→<sup>3</sup>T<sub>1g</sub>(P) respectively which were characteristic of their octahedral geometry[22]. The diamagnetic Zn(II) complexes spectra are dominated only by charge transfer bands. The charge transfer bands at 370nm and 435nm in the complexes are characteristic of octahedral environment. [23]The Cu (II) complexes show intense bands around 330 nm assigned to the intramolecular charge transfer of the ligand to metal. The band at 621nm can be attributed to a d→ d transitions which corresponds to octahedral geometry. The broadness of band arises due to ligand field and Jahn Teller distortion and in a typical d<sup>9</sup> system. Though three transitions are expected, they are very close in energy and often appear in the form of one broad band envelope [24]. The EPR spectra of the Ni(II) complexes of en, dien and trien show two signals corresponding to g<sup>⊥</sup> 2.00 and g<sup>||</sup> 1.948. It is evident from the perpendicular signal that there is coupling with two nitrogen atoms which resulted in the quintet in the ratio 1:2:3:2:1. All the complexes thus have a near Oh arrangement about Ni (II) with two chelated pmdtc units and adiamine coordinating through two NH<sub>2</sub> Nitrogen atoms. The EPR spectra of Cu (II) complexes of en, dien and trien show only one intense signal corresponding to g 2.04. As the Zn (II) complexes were diamagnetic in nature. The Proton NMR Spectra of Zn (II) complexes were studied. The piperidine ring in zinc complexes gives three signals due to the presence of three nonequivalent sites. The singlet at 4.1ppm is due to the protons present ortho to the nitrogen in piperidine ring. The signals that appear around 3.6ppm is due to the protons present in the Meta position. The protons in the para position appear at 2.5ppm. All the signals appear a little downfield due to delocalization of the electron density in the S- C=S linkage. The CH<sub>2</sub>protons of the (en/dien/trien) appear around 1.6ppm. The magnetic susceptibility studies of Ni (II) complexes shows an increase in mass in the presence of magnetic field. The VSM plot of magnetic moment in emu vs. field shows hysteresis loop indicating ferromagnetism and negligible height loops and the coercivity suggest that these complexes have significantly small size whereas the VSM Plot of Cu (II) complexes indicated paramagnetism.

### IV. Biological studies

Antibacterial studies of all the nine complexes were studied by using the disc diffusion method which indicated that the complexes have moderate activity against all the five bacteria studied namely Staphylococcus aureus, Aeromonas spp, Bacillus subtilis, E. coli and Vibrio parahaemolyticus compared to the standard antibiotic ampicillin. The diameter of the inhibitory zone from anti-bacterial studies are presented in Table III. The en analog Ni (II) do not show activity even at high concentration for Vibrio parahaemolyticus, whereas dien and trien analogues of Ni (II) show better activity towards all the five bacteria tested. The trien analog of Zn (II) and en, trien analogues of Cu (II) do not show any activity at lower concentrations, but with increase in concentrations, they shows only moderate activity. The Cu complexes of en, dien and trien do not show any activity towards E. coli even at higher concentrations. The Cu (II) en and trien complexes do not show activity at low concentration for Candida albicans and Trichoderma viridewhileas dien complex were active even at low concentration. As seen from the data Cu (II) complexes have better antifungal activity when compared to Ni (II) and Zn (II) complexes.

The anticancer activities of these complexes were studied using MTT assay method on MCF-7 cell line and was compared against the VERO cell line. All the nine complexes show considerable activity against the cancer cells but seems to have less toxicity towards normal cells. The IC<sub>50</sub> values of en, dien and trien complexes of Ni are 15.6, 31.2, 7.8 and those of Cu are 15.6, 31.2, 15.6 and finally those of Zn are 15.6, 31.2, 15.6 respectively. The above data indicates the en complexes have highest activity and the activity falls as we move to dien complexes. However the activity increases with trien in case of Ni, Cu and Zn. Mere anticancer activity cannot be significant and it is necessary to check the damage to normal cells. The selectivity index [Selectivity index = IC<sub>50</sub> for normal cell line / IC<sub>50</sub> for cancerous cell line][25] is a better index to understand the significance of anticancer agents. This selectivity index for en dien and trien complexes of Ni are 8, 4, 8 and those of Cu are 32, 8, 32 and those of Zn are 32, 16, and 32. The Zn and Cu complexes with greater selectivity index (16, 32) indicated excellent anticancer activity towards MCF-7 cell line when compared to Ni complex.

**Table-I** Elemental composition and Electronic spectral data (nm)

Complexes	Colour	%N (theo) exp	%s (theo) Exp	%Metal (theo) Exp	λmax	Residue% TGA (theo) exp
[Ni(en)(pmdtc) <sub>2</sub> ]	Green	(12.70) 11.72	(29.04) 28.72	(13.31) 12.80	632, 440,320	(20.6) 19.58
[Ni(dien)(pmdtc) <sub>2</sub> ]	Green	(14.44) 13.89	(26.41) 26.21	(12.10) 12.02	645, 440,304	(18.7) 18.09
[Ni(trien)(pmdtc) <sub>2</sub> ]	Green	(15.94) 15.13	(24.29) 23.56	(11.13) 10.82	639 440,305	(17.2) 17.03
[Zn(en)(pmdtc) <sub>2</sub> ]	White	(12.51) 11.43	(28.61) 28.34	(14.62) 14.23	435,370	(21.6) 21.12
[Zn(dien)(pmdtc) <sub>2</sub> ]	White	(14.24) 13.32	(26.05) 25.75	(13.31) 13.26	435,367	(19.8) 19.37
[Zn(trien)(pmdtc) <sub>2</sub> ]	White	(15.74) 15.23	(23.98) 23.03	(12.25) 11.35	435,372	(18.2) 18.09
[Cu(en)(pmdtc) <sub>2</sub> ]	Brown	(12.56) 12.13	(28.72) 27.89	(14.21) 14.07	339,617	(21.4) 21.12
[Cu(dien)(pmdtc) <sub>2</sub> ]	Brown	(14.30) 13.28	(26.14) 25.65	(12.92) 12.56	339,621	(19.5) 19.0
[Cu(trien)(pmdtc) <sub>2</sub> ]	Brown	(16.05) 15.98	(24.46) 23.45	(12.13) 11.88	339,609	(18.2) 18.0

**Table-II** IR spectral data

Complexes	vN-H	vC-H piperdine	vC-H amine	vC=s	vC-S	vN-C
[Ni(en)(pmdtc) <sub>2</sub> ]	3431	2937	2850	1234	950	1363
[Ni(dien)(pmdtc) <sub>2</sub> ]	3425	2929	2850	1236	960	1359
[Ni(trien)(pmdtc) <sub>2</sub> ]	3423	2933	2850	1230	964	1355
[Zn(en)(pmdtc) <sub>2</sub> ]	3426	2937	2851	1220	954	1359
[Zn(dien)(pmdtc) <sub>2</sub> ]	3424	2931	2850	1232	953	1356
[Zn(trien)(pmdtc) <sub>2</sub> ]	3425	2938	2852	1238	946	1352
[Cu(en)(pmdtc) <sub>2</sub> ]	3427	2929	2850	1233	957	1357
[Cu(dien)(pmdtc) <sub>2</sub> ]	3435	2930	2850	1229	956	1356
[Cu(trien)(pmdtc) <sub>2</sub> ]	3440	2929	2850	1235	959	1359

v cm<sup>-1</sup>

**Table-III** Antibacterial Studies:

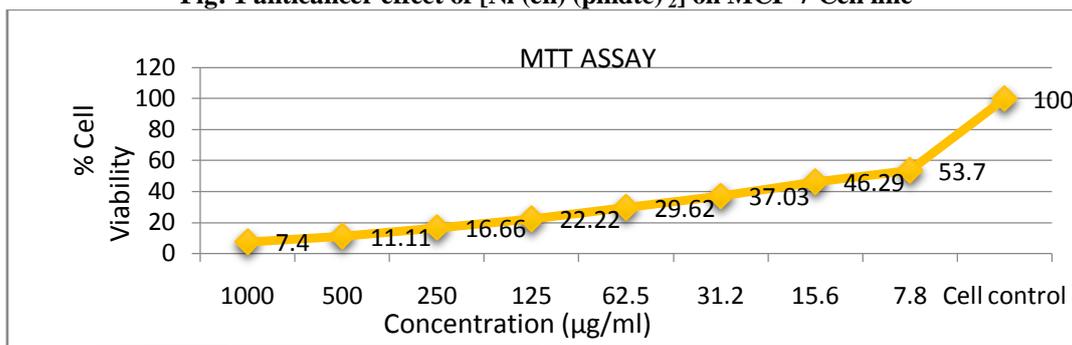
Complexes	Organisms	Zone of inhibition(mm)			Antibiotic (1mg/ml)
		Concentration(µg/ml)			
		1000	750	500	
[Ni(en)(pmdtc) <sub>2</sub> ]	E.coli	8mm	7mm	6mm	10mm
	AeromonasSpp	9mm	8mm	7mm	11mm
	Staphylococcus aureus	10mm	8mm	7mm	15mm
	Vibrio Parahemolyticus	-	-	-	12mm
	Bacillus Subtilis	8mm	7mm	6mm	15mm
[Ni(dien)(pmdtc) <sub>2</sub> ]	E.coli	8mm	7mm	5mm	11mm
	AeromonasSpp	9mm	7mm	6mm	11mm
	Staphylococcus aureus	8mm	7mm	6mm	15mm
	Vibrio Parahemolyticus	7mm	6mm	5mm	16mm
	Bacillus Subtilis	9mm	8mm	6mm	17mm
[Ni(trien)(pmdtc) <sub>2</sub> ]	E.coli	9mm	8mm	6mm	13mm
	AeromonasSpp	8mm	7mm	5mm	12mm
	Staphylococcus aureus	9mm	7mm	6mm	16mm

	Vibrio Parahemolyticus	8mm	7mm	5mm	15mm
	Bacillus Subtilis	9mm	8mm	7mm	16mm
[Zn(en)(pmdtc) <sub>2</sub> ]	E.coli	-	-	-	8mm
	AeromonasSpp	10mm	9mm	8mm	13mm
	Staphylococcus aureus	9mm	-	-	15mm
	Vibrio Parahemolyticus	12mm	10mm	7mm	14mm
	Bacillus Subtilis	10mm	8mm	6mm	15mm
[Zn(dien)(pmdtc) <sub>2</sub> ]	E.coli	8mm	-	-	11mm
	AeromonasSpp	10mm	8mm	7mm	12mm
	Staphylococcus aureus	9mm	7mm	6mm	15mm
	Vibrio Parahemolyticus	10mm	9mm	7mm	14mm
	Bacillus Subtilis	9mm	-	-	16mm
[Zn(trien)(pmdtc) <sub>2</sub> ]	E.coli	11mm	8mm	7mm	12mm
	AeromonasSpp	8mm	-	-	13mm
	Staphylococcus aureus	10mm	8mm	-	14mm
	Vibrio Parahemolyticus	9mm	-	-	10mm
	Bacillus Subtilis	10mm	8mm	-	14mm
[Cu(en)(pmdtc) <sub>2</sub> ]	E.coli	-	-	-	10mm
	AeromonasSpp	11mm	9mm	-	14mm
	Staphylococcus aureus	9mm	7mm	-	14mm
	Vibrio Parahemolyticus	10mm	9mm	8mm	14mm
	Bacillus Subtilis	10mm	-	-	15mm
[Cu(dien)(pmdtc) <sub>2</sub> ]	E.coli	-	-	-	9mm
	AeromonasSpp	-	-	-	13mm
	Staphylococcus aureus	11mm	8mm	7mm	15mm
	Vibrio Parahemolyticus	10mm	8mm	7mm	13mm
	Bacillus Subtilis	9mm	8mm	6mm	16mm
[Cu(trien)(pmdtc) <sub>2</sub> ]	E.coli	-	-	-	7mm
	AeromonasSpp	-	-	-	12mm
	Staphylococcus aureus	10mm	8mm	-	14mm
	Vibrio Parahemolyticus	10mm	8mm	7mm	17mm
	Bacillus Subtilis	9mm	8mm	-	14mm

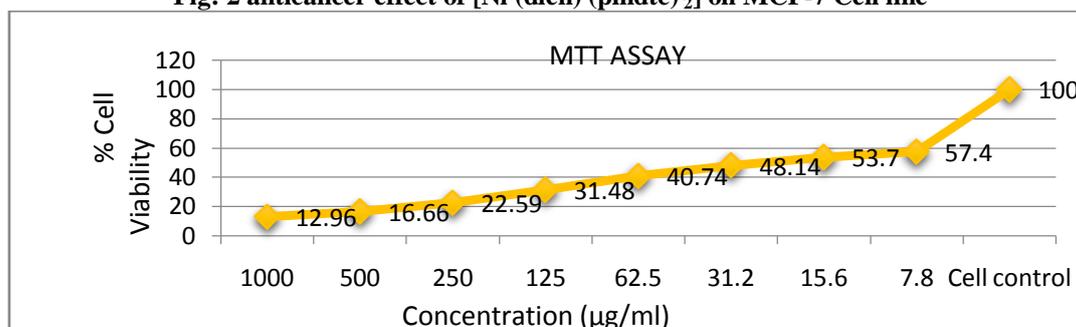
**Table-IV** Antifungal Studies

Complexes	Organisms	Zone of inhibition(mm)			Antibiotic (1mg/ml)
		Concentration(µg/ml)			
		1000	750	500	
[Ni(en)(pmdtc) <sub>2</sub> ]	Candida albicans	10mm	7mm	6mm	12mm
	Trichoderma Viridi	9mm	8mm	6mm	11mm
	Aspergillusniger	-	-	-	8mm
[Ni(dien)(pmdtc) <sub>2</sub> ]	Candida albicans	9mm	-	-	11mm
	Trichoderma Viridi	10mm	9mm	-	12mm
	Aspergillusniger	8mm	-	-	12mm
[Ni(trien)(pmdtc) <sub>2</sub> ]	Candida albicans	8mm	-	-	10mm
	Trichoderma Viridi	10mm	7mm	-	12mm
	Aspergillusniger	8mm	6mm	-	12mm
[Zn(en)(pmdtc) <sub>2</sub> ]	Candida albicans	9mm	8mm	7mm	13mm
	Trichoderma Viridi	9mm	7mm	-	12mm
	Aspergillusniger	9mm	7mm	-	13mm
[Zn(dien)(pmdtc) <sub>2</sub> ]	Candida albicans	9mm	8mm	7mm	12mm
	Trichoderma Viridi	12mm	9mm	7mm	14mm
	Aspergillusniger	9mm	-	-	13mm
[Zn(trien)(pmdtc) <sub>2</sub> ]	Candida albicans	10mm	8mm	-	12mm
	Trichoderma Viridi	10mm	8mm	6mm	15mm
	Aspergillusniger	9mm	-	-	13mm
[Cu(en)(pmdtc) <sub>2</sub> ]	Candida albicans	8mm	7mm	-	11mm
	Trichoderma Viridi	11mm	8mm	7mm	13mm
	Aspergillusniger	10mm	8mm	7mm	13mm
[Cu(dien)(pmdtc) <sub>2</sub> ]	Candida albicans	10mm	9mm	8mm	13mm
	Trichoderma Viridi	10mm	8mm	7mm	13mm
	Aspergillusniger	10mm	8mm	7mm	14mm
[Cu(trien)(pmdtc) <sub>2</sub> ]	Candida albicans	7mm	-	-	11mm
	Trichoderma Viridi	9mm	8mm	6mm	13mm
	Aspergillusniger	9mm	-	-	13mm

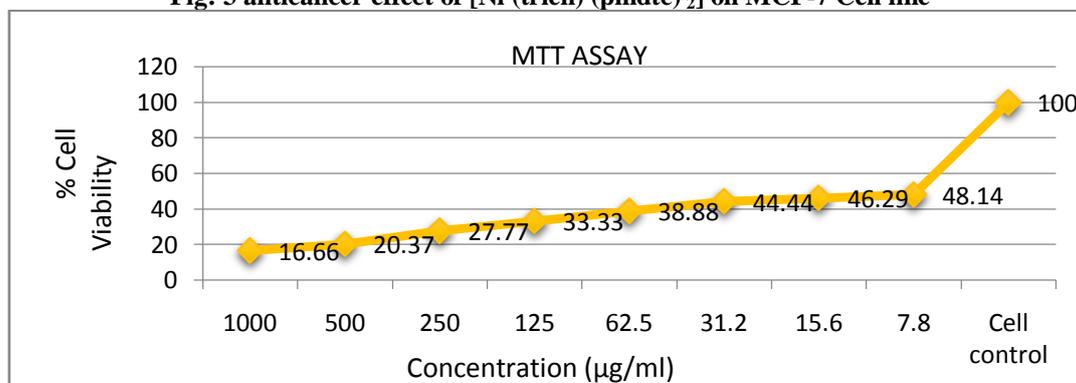
**Fig: 1 anticancer effect of [Ni (en) (pmdtc)<sub>2</sub>] on MCF-7 Cell line**



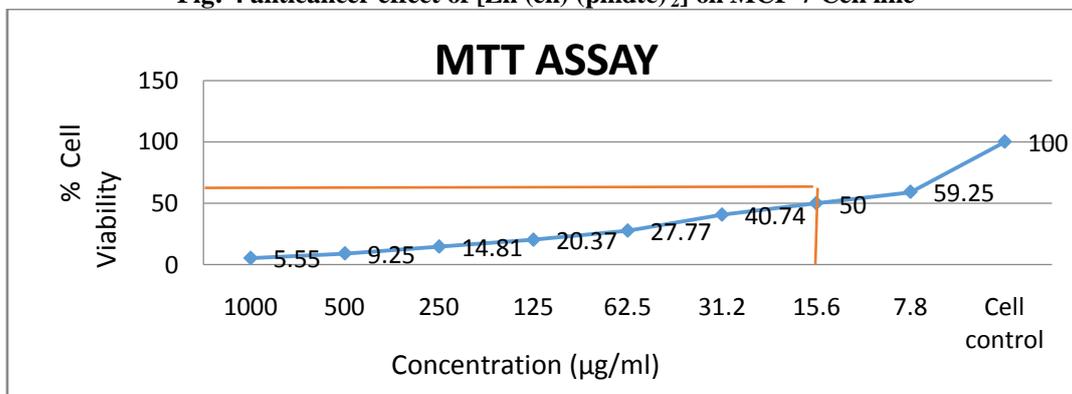
**Fig: 2 anticancer effect of [Ni (dien) (pmdtc)<sub>2</sub>] on MCF-7 Cell line**



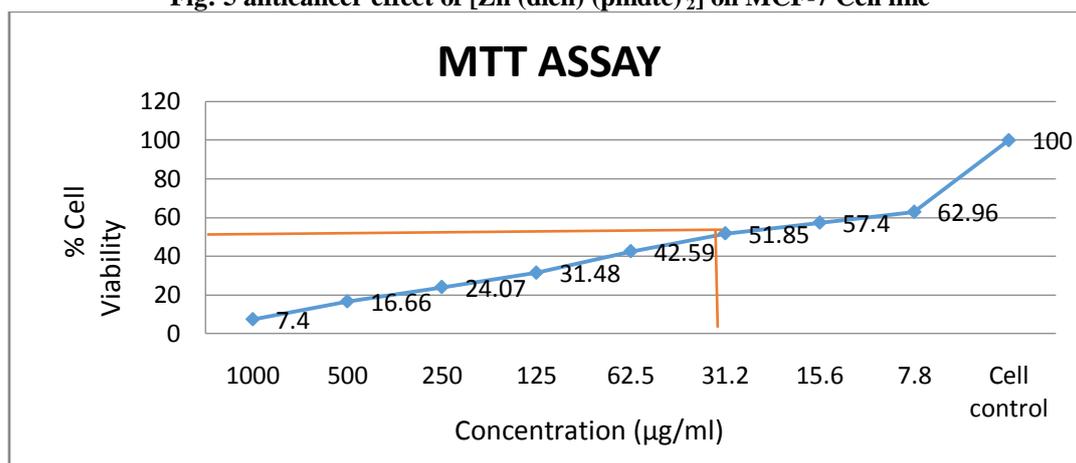
**Fig: 3 anticancer effect of [Ni (trien) (pmdtc)<sub>2</sub>] on MCF-7 Cell line**



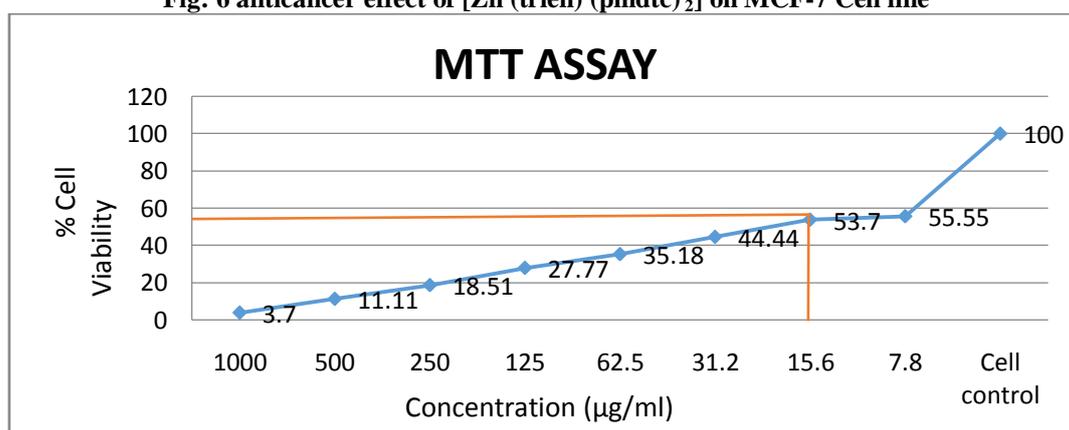
**Fig: 4 anticancer effect of [Zn (en) (pmdtc)<sub>2</sub>] on MCF-7 Cell line**



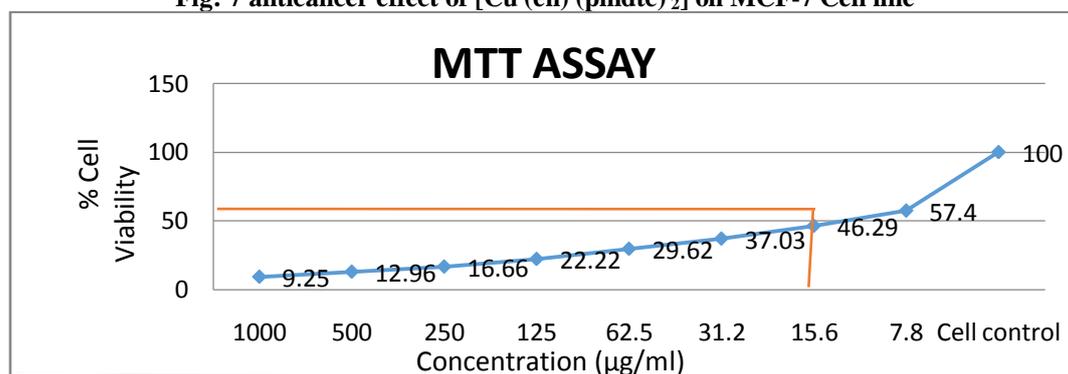
**Fig: 5 anticancer effect of [Zn (dien) (pmdtc)<sub>2</sub>] on MCF-7 Cell line**



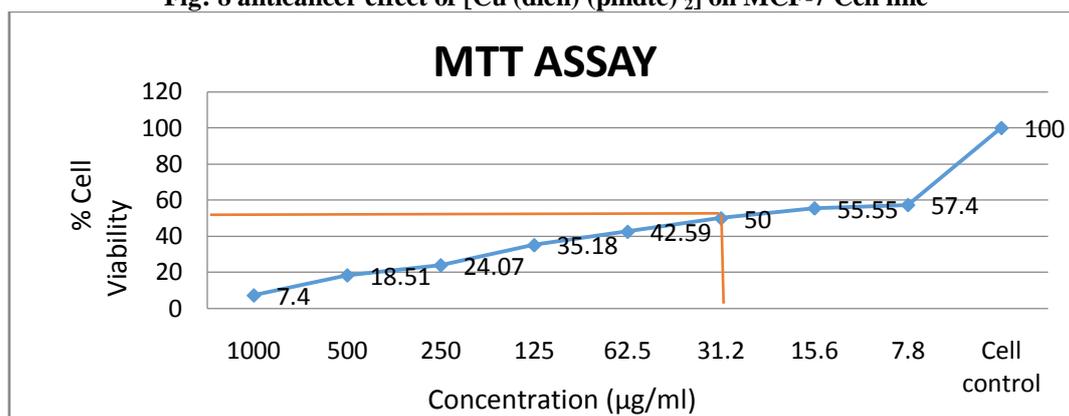
**Fig: 6 anticancer effect of [Zn (trien) (pmdtc)<sub>2</sub>] on MCF-7 Cell line**



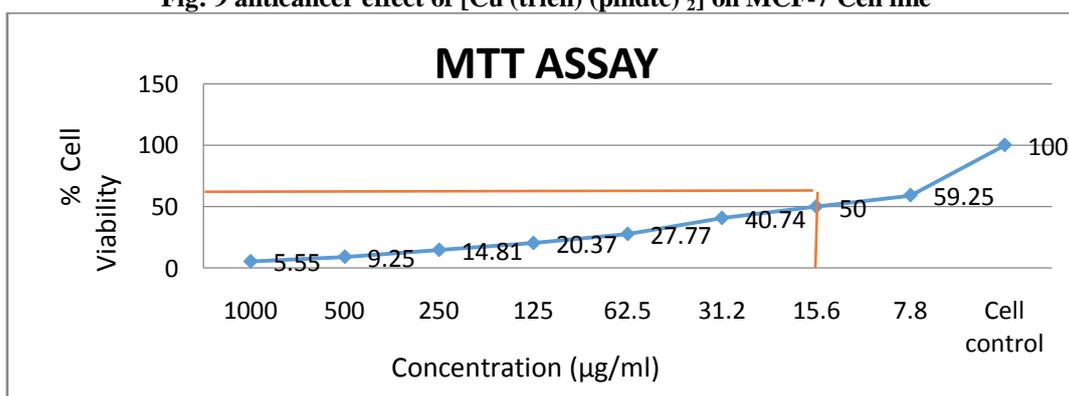
**Fig: 7 anticancer effect of [Cu (en) (pmdtc)<sub>2</sub>] on MCF-7 Cell line**



**Fig: 8 anticancer effect of [Cu (dien) (pmdtc)<sub>2</sub>] on MCF-7 Cell line**



**Fig: 9 anticancer effect of [Cu (trien) (pmdtc)<sub>2</sub>] on MCF-7 Cell line**



## V. Conclusion

The antimicrobial studies of these complexes have shown reasonable activity towards some of the tested microorganisms and shows promising applications in the field of medicines. The anticancer activity of en and trien complexes of Zn and Cu with higher selectivity index opens a new area of research of these complexes as anticancer therapeutic drugs.

## Acknowledgement

The authors acknowledge the Department Of Chemistry and Instrumentation Centre Ethiraj College for Women, Chennai-8, for the facilities provided and IIT-Madras (SAIF) for recording various spectra.

## References

- [1]. Onwudiwe DC, AjibadePA, Synthesis, Characterization and Thermal Studies of Zn (II), Cd (II) and Hg (II) Complexes of N-Methyl-N-Phenyldithiocarbamate: The Single Crystal Structure of [(C<sub>6</sub>H<sub>5</sub>) (CH<sub>3</sub>) NCS<sub>2</sub>]<sub>4</sub>Hg<sub>2</sub>, Int.J.Mol.Sci 12, 2011, 1964-1978.
- [2]. Onwudiwe, D.C; Ajibade, P.A. Synthesis and characterization of metal complexes of N-alkyl-N-phenyl dithiocarbamates, Polyhedron, 29, 2010, 1431-1436.
- [3]. Benigno, M.; María, V.V.; Eduardo, C.; Silvia, M.V.; Alfonso, C.; Joaquín, B. Copper complexes with dithiocarbamates derived from natural occurring amino acids. Crystal and molecular structure of [Cu(en)(EtOH)(H<sub>2</sub>O)<sub>3</sub>][Cu(dtc-pro)<sub>2</sub>], Polyhedron, 2002, 21, 1899-1904.
- [4]. De Lima, M.; Menezes, C.; Camila, A.C.; Jaqueline, A.F.; dos Santos; Isabella, P.F.; Eucler, B.P.; James, L.W.; Solange, M.S.; Wardell, K.K.; Isolda, C.M.; Heloisa, B. Synthesis, characterization and biological aspects of copper(II) dithiocarbamate complexes, [Cu{S<sub>2</sub>CNR(CH<sub>2</sub>CH<sub>2</sub>OH)}<sub>2</sub>], (R = Me, Et, Pr and CH<sub>2</sub>CH<sub>2</sub>OH). J.Mol. Struct., 2011, 988, 1-8.
- [5]. Saad E. Al- Mukhtar et al, Synthesis and Characterization of Mn(II), Fe(II) and Co(II) Complexes with 4-Hydroxypiperidinedithiocarbamate and their Adducts with Neutral Bases, Raf. J. Sci., 2014, Vol. 25, 53-61, 2014.
- [6]. Marcotrigiano et al. The synthesis and properties of cobalt (II), nickel (II) and Copper (II) complexes with some hetero cyclic dithiocarbamates. InorgChemActa., 1984; 86, 127-131.
- [7]. A.J.Odola and J.A.O.Woods, New Nickel(II) mixed ligand complexes of dithiocarbamate with schiffbase, Journal Of Chemical and Pharmaceutical Research, 2011, 3, 865-871.
- [8]. Leka Z.B, Leovac V.M, Lukic S, Sabo T.J, Trifunovic S.R and Katalin M.S. Synthesis and physico-chemical characterization of new dithiocarbamate ligand and its complexes with copper(II), nickel(II) and Palladium(II). J. Therm Anal and Cal; 2006; 83.
- [9]. A. M. Hamil et al, synthesis, Spectroscopic investigation and Antiactivity of Schiff base complexes of Co (II) and Cu (II) ions, RasayanJournal.chem, 2009, Vol.2, No. 261-266
- [10]. Rathore, H.S.; Varshney, G.; Mojumdar, S.C.; Saleh, M.T. Synthesis, characterization and fungicidal activity of zinc diethyldithiocarbamate and phosphate. Ther. Anal. Calorim, 2007, 90 (3), 681-686.

- [11]. Shaheen, F.; Badshah, A.; Gielen, M.; Dusek, M.; Fejfarova, K.; De Vos, D.; Mirza, B. Synthesis, characterization, antibacterial and cytotoxic activity of new palladium(II) complexes with dithiocarbamate ligands: X-ray structure of bis(dibenzyl-1-S: S'-dithiocarbamate) Pd(II). *J. Organomet. Chem.* 2007,692, 3019–3026.
- [12]. Montagner, D.; Marzano, C.; Gandin, V. Synthesis, characterization and cytotoxic activity of palladium (II) dithiocarbamate complexes with an x-diamines. *Inorg.Chem. Acta.*, 2011, 376, 574–580.
- [13]. Faraglia G, Fregona D , Sitran S , Giovagnini L , Marzano C, Baccichetti F, Casellato , Graziani., Mixed Pt(ii) and palladium (ii) dithiocarbamate complexes and amines: synthesis , characterisation and cell assay., *J.Inorg.Biochem.*2001;83:31-40.
- [14]. H.Nabipour, Synthesis of a new dithiocarbamate cobalt complex and its nanoparticles with the study of their biological properties, *Intl.J.Nano.dimn*, 2011, 1(3); 225-232.
- [15]. Hogarth, G. (2005). Transition Metal Dithiocarbamates: 1978-2003. *Progress in Inorganic Chemistry* 53, 71-561.
- [16]. Morf.P.;Raimondi,F.;Nothofer.H.-G.;Schnyder,B.;Yasuda,A.;Wessels,J.M.;Jung,T.A.; Dithiocarbamates: functional and versatile linkers for the formation of self-assembled monolayers,*Langmuir* ;2006,22,658-663.
- [17]. A.W.Bauer et al Antibiotic Susceptibility Testing by a Standardized Single Disc Method, *.Am.J.Clin.Pathol.*1966, 36,493.
- [18]. T.Mossman, Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays.*J.Immunol Methods*, 1883, 65, 55.
- [19]. BharathiKrishnan,R.Vijayanthimala,Synthesis, Characterisation and Biological Applications of mixed ligand Cobalt (II) Complexes containing Dithiocarbamates and Diamines,*International Journal of chemical and pharamaceutical sciences*,2015,6,36-40.
- [20]. Geary W.J., The use of conductivity measurements in organic solvents for the characterisation of coordination compounds. , *Coord.Chem. Rev.*, 1971, 7, 81.
- [21]. Layla. J.N.et al, Synthesis and Characterization of Some Metal (II) Complexes of Dithiocarbamate,*Tikrit Journal of Pure Science* 18 (3) 2013,1813 – 1662.
- [22]. CezarSpinu, Angela Kriza; Co (II), Ni (II) and Cu (II) Complexes of bidentateschiff bases; *ActaChim. Slov*, 2000, 47, 179-185.
- [23]. F.A Cotton and G Wilkinson; *Advanced inorganic chemistry* fourth edition; John Wiley and sons New York; 1980; pp 61-71, 786-791.
- [24]. Abeer A. Alhadi1, Shayma A. Shaker, Wagee A. Yehye1, HapipahMohd Ali1 and Mahmood A. Abdullah,Synthesis, magnetic and spectroscopic studies of Ni(II), Cu(II), Zn(II)and Cd(II) complexes of a newly Schiff base derived from 5-bromo-2-hydroxybezylidene-3,4,5-trihydroxybenzohydrazide,*Bull. Chem. Soc. Ethiop.* 2012, 26(1), 95-101.
- [25]. Ramesh B.Badisa,Selina f Darling-Reed, Patrick Joseph, John S. Cooperwood,Lekan M. Latiwo,Carl B. Goodman;Selective Cytotoxic Activities of two Novel synthetic Drugs on Human Breast Carcinoma MCF-7 Cells;*Anticancer Research*;2009;29;2993-2996.