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Template synthesis, characterization, biological screening of Cr (III) and Fe (III) tetraaza macrocyclic complexes derived from 9, 10-phenanthrenequinone and 1, 3-dicarbonyl-phenyl-dihydrazide

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ABSTRACT

In the present article macrocyclic ligand of type ($C_{22}H_{14}N_4O_2$) and its transition metal complexes of type[M($C_{22}H_{14}N_4O_2$)X_2]X, where M=Cr(III), and Fe(III), X = Cl^-, NO_3^- and CH_3COO^- have been synthesized by template condensation of 1,3-dicarbonyl-phenyl-dihydrazide and 9,10-phenanthrenequinone(PhQ) in methanolic medium in 1:1:1 molar ratio. The structure and geometry of synthesized complexes and ligand is proposed on the basis of various modern physicochemical characterization techniques (spectral, thermal) and found to be six coordinated octahedral geometry of all the synthesized species. Ligand is coordinated to metal in a tetradentate manner in all complexes. Molar conductance measurements showed that reported macrocyclic complexes are weakly electrolytic in nature. All the synthesized compounds have been tested for their in vitro antibacterial activity against two gram +ve and two gram -ve pathogenic bacterial strains viz. Staphylococcus aureus, Bacillus cereus (gram +ve) and Salmonella typhi, E.Coli(gram -ve) to access their inhibiting potential. The results obtained were compared with the standard antibacterial drug Ciprofloxacin. The antiradical activity of some newly synthesized complexes has also been evaluated by using DPPH radical scavenging method and compared with standard antioxidant Ascorbic acid.

Keywords: Antioxidant, Antibacterial, Macrocyclic complex, Bacillus cereus, DPPH

INTRODUCTION

Macrocyclic complexes have attracted the attention of researchers because of their role in biological and molecular processes[1-3].In last few years extensive research has been aimed to design new and highly effective synthetic macrocyclic metal complexes [4-13] because of their close relationship with naturally occurring macrocyclic molecules[14-16].Transition metal macrocyclic complexes have been extensively studied by researchers in search of designing new chemical agents because of their excellent biological activities, including antimicrobial, anticarcinogenic, and antioxidant etc. [17-19].

These compounds have shown remarkable bacterial inhibiting potential either by penetrating through bacterial cell wall to inactivate their enzymes or by generating H_2O_2 and kill the bacteria. Presence of metal ions accelerates the drug action and efficiency of organic therapeutic agents. The structure and geometry of coordination compounds also influence their antibacterial action with other factors like thermodyanamic stability, hydrolytic stability , kinetics of ligation, molecular weight etc. to release the metal ion to desired active site[20-23].

Template condensation method of complex formation has been very popular where metal ions are used as the templating agent [20] and facilitate the formation of cyclic products by providing selective route to reaction [21-23] which is not possible in the absence of metal ion.

Metal complexes based on hydrazone unit have been displayed wide range of biological and pharmaceutical activities [24] because of the formation of –CONH- linkage which is a useful building unit for peptides formation from amino acids in biological systems. It also gives higher stability to the molecules because of the presence of a chelatophore group of donor atoms in the coordination sphere [25-28].The coordination abilities of these ligands have attracted our attention and aroused our interest in elucidating new structures and evaluating their antimicrobial potential as new therapeutic agents are always sought.

Research work represents the preparation and characterization of the chemical structures derived from the condensation of 1,3-dicarbonyl-phenyl-dihydrazide and 9,10-phenanthrenequinone with transition metals and also evaluate their antibacterial properties against various pathogenic strains of bacteria. The complexes were also checked and evaluated for their antioxidant ability as it becomes great if the compounds are good antimicrobial as well as good antioxidant.

MATERIALS AND METHODS

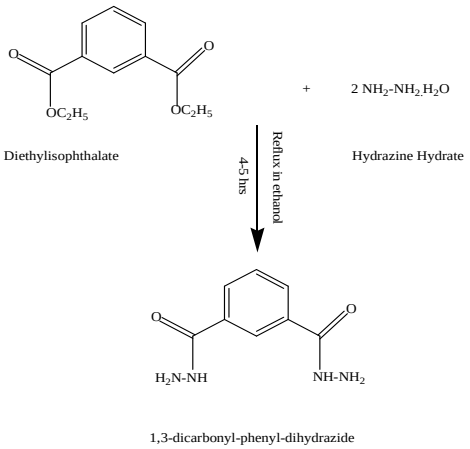
2.1Materials

All the chemicals and solvents used in this study were of AR grade. Diethyl Isophthalate, 9,10-phenanthrenequinone and 98% hydrazine hydrate were purchased from Sigma(USA) and Aldrich(Germany).

The metal salts were purchased from S.D. fine, Mumbai India, Merck, Ranbaxy, India, and were used as received. Solvents like methanol, ethanol and ether were used as such without any distillation.

2.2Synthesis of precursor 1,3-dicarbonyl-phenyl-dihydrazide

Hydrazine hydrate (98% 2 cc) was added to a hot stirring ethanolic solution of Diethylbenzene-1,3-dicarboxylate (0.01mole, 2.22 g) and refluxed for 4–5 h at 35-40^{0}C. The reaction mixture was then allowed to cool at room temperature; a white coloured precipitate was formed. The cooled precipitate was filtered through the crucible and washed with ethanol and ether. Precipitate was allowed to dry in air and then put into dessicator for further use.

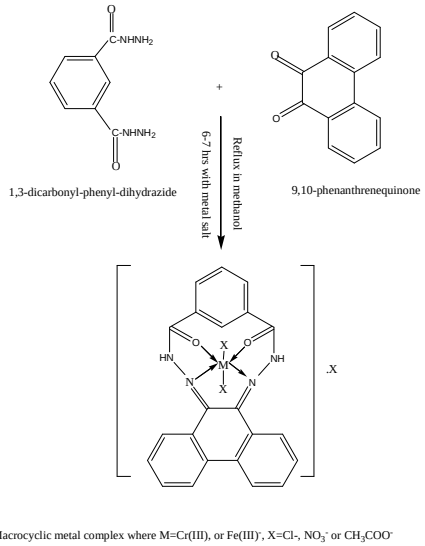


Scheme 1: Synthesis of 1,3-dicarbonyl-phenyl-dihydrazide

2.3 Isolations of complexes

A calculated amount of 1,3-dicarbonyl-phenyl-dihydrazide (0.01mol,2.52gm) and corresponding trivalent metal salt(0.01mol) was dissolved in methanol(50 ml) with continuous stirring and 4-5 drops of dil. HCl was added. The resulting solution was refluxed at 35-40^{0}C for half an hour. Subsequently a solution of 9, 10-phenanthrenequinone (0.01mol, 2.08gm) in 20 ml ethanol was added to it and continuously refluxed for 6–7 hours at 35-40^{0}C. The mixture was then concentrated to half of its volume through evaporation. Dark colored precipitates were appeared,

filtered, washed with methanol, acetone and diethyl ether and dried *in vacuum*. The obtained yields were ≈ 60—65 %. The complexes were only soluble in DMF and DMSO. Scheme 2



Macrocyclic metal complex where M=Cr(III), or Fe(III)$^{+}$, X=Cl-, NO_3^- or CH_3COO^-

Scheme 2: Synthesis of metal macrocyclic complex [MLX_2].X derived from 1,3-dicarbonyl-phenyl-dihydrazide and 9,10-phenanthrenequinone in the presence of trivalent metal salts

2.5Analytical and physical measurements

The microanalysis for C, H, and N, O, and M was realized using an elemental analyzer (Perkin Elmer 2400) at IIT Delhi. The magnetic susceptibility measurements of the compounds were carried out by Gouy balance at room temperature. The IR spectra were recorded on Thermo Scientific Nicolet S 50 FT-IR Spectrometer in the range 4000-400 cm^{-1} using ATR. UV-Visible spectra in DMSO were recorded on PerkinElmer Lambda 25 spectrophotometer ranging 200-900nm. The molar conductance was measured on digital conductivity meter (HPG system, G-3001). The metal contents in the complexes were determined by Atomic absorption spectroscopy (Perkin Elmer 5000).ESI Mass spectra were obtained from JEOL-ACCU TOF JMS-T100LC mass spectrometer ranging 50.0-1000.0.Thermal analysis of complexes was carried out by TGA Perkin Elmer thermo analyzer. The ^{1}H NMR spectra was recorded at room temperature in DMSO on a Bruker AVANCE II 400 NMR spectrometer (400 MHz) from IIT Delhi

Melting points were determined by using capillaries in electrical melting point apparatus.

2.6 In vitro antibacterial activity

All the newly synthesized complexes were evaluated for their antibacterial activities towards

Staphylococcus aureus & Bacillus cereus (gram +ve), Salmonella typhi & E.coli (gram –ve) by using Agar well diffusion method. Bacterial cultures were procured from microbial type culture collection IMTECH Chandigarh and subcultured on nutrient agar media.

The qualitative and quantitative analysis of antibacterial potential of the newly synthesized ligand and its metal complexes against all bacterial strains has been studied by Agar well diffusion method [29].

For qualitative analysis, a microbial suspension of approximately $1X10^7$ cfu/ml (0.5 McFarland) from a 24hr old culture was used. 20 ml of MHA was poured into each sterile petri plates, 100 ml inocula of the test microbe was swabbed onto each petri plate which is loaded with nutrient agar media (agar 20g+ peptones 5g+beef extract 3g) and kept for 30 minutes for incubation (adsorption).Wells were bored using sterile borer (6mm), into the nutrient agar loaded and seeded petri plates. These bores were loaded with 100ml of the test compound at concentration 1.0mg/ml prepared in DMSO. 75 ml of seeded nutrient agar was poured onto each petri plate and incubated for 24 hrs at 37^0C.

Measurement of diameter of bacterial growth inhibition zones in mm for each test compound was used for quantitative analysis.

For the detection of MIC the macro dilution broth method was performed [30]. Serial dilutions of all test compounds ranging 512-16 µg /ml in DMSO were prepared within sterile tubes. Test compound containing tubes were inoculated with a standardized bacterial suspension of all strains with 10^7 cfu mL^{-1} concentration. DMSO was used as negative control. Tubes were incubated for 24 hrs and MIC for all test compounds and standard antibiotic was observed.

2.7Antiradical activity

Free radical induced oxidative damage of DNA in humans is well known problem [31] so antiradical potential of some of the synthesized compound was investigated using DPPH method [32].

Stock solution of 10^{-3}M of DPPH was prepared in methanol and the solutions of all test compounds of concentration 0,100, 250 &500 µg/ml were prepared in DMF. To 1 ml of sample solution, 3 ml of methanolic solution of DPPH (10^{-3}M) was added and kept for 30 min for incubation at room temperature [32].

Free radical scavenging potential of synthesized complexes was observed by measuring their absorbance at 517nm at room temperature.

RESULTS AND DISCUSSION

3.1Analytical and physical measurement

The analytical data showed the suggested formula for macrocyclic complexes as: [M **$[C_{22}H_{14}N_4O_2]$** X_2]X, where M = Cr (III), Fe (III), X = Cl^-, NO_3^- or CH_3COO^- and $[C_{22}H_{14}N_4O_2]$ corresponds to the tetradentate macrocyclic ligand. The analysis also suggest a 1:1 stoichiometry for all synthesized complexes The metal complexes were dissolved in DMF and molar conductivities of 20 ml of 10^{-3} M of their solutions were measured at room temperature. All the complexes showed molar conductance 60-80 Ω^{-1} cm^2 mol^{-1}. It was concluded from the results that complexes are weakly electrolytic in nature [33]. Therefore, these complexes may be formulated as $[MLX_2].X$ however various analytical, spectroscopic and magnetic studies enabled the possible structure of the synthesized complexes to be predicted.

All complexes gave satisfactory micro elemental analyses results, as shown in Table I.

Table 1: Physical properties i.e. Molar conductance, molecular weight and elemental analysis of all synthesized species

Mol. Formula	Melting point(^{0}C)	Colour	%Yield	Mol. Weight based on formula	Elemental analysis, Calculated(found)				
					C	H	N	O	M
$C_{22}H_{14}N_4O_2$ = L compound 1	265	Light brown	20%	366	72.12 (71.15)	3.85 (3.2)	15.29 (15.1)	8.73 (8.96)	-
$[Cr(L)(OAc)_2]OAc$ compound 2	295	Yellowish green	64%	595.4	56.4 (55.7)	3.8 (3.6)	9.4 (9.3)	21.4 (20.9)	8.73 (8.67)
$[Cr(L)(NO_3)_2]NO_3$ Compound 3	290	Green	62%	604	43.7 (42.5)	2.33 (2.30)	16.2 (15.98)	29.1 (28.9)	8.6 (8.4)
$[Cr(L)Cl_2]Cl$ Compound 4	275	Yellow green	60%	524.7	50.3 (50.1)	2.69 (2.6)	10.6 (10.2)	20.2 (20.1)	6.1 (6.0)
$[Fe(L)(OAc)_2]OAc$ compound 5	280	Brown	60%	599.3	56.1 (55.98)	3.8 (3.5)	9.3 (9.0)	21.3 (21.1)	9.32 (9.2)
$[Fe(L)(NO_3)_2]NO_3$ Compound 6	283	Red brown	62%	608	43.4 (43.1)	2.3 (2.1)	16.1 (15.9)	28.9 (28.6)	9.18 (9.08)

3.2 Infra- red spectral Analysis

To understand the binding mode of ligand to metal in complexes, IR peaks obtained for free ligand and its metal complexes were compared successfully. Ligand gave three specific IR absorption peaks in IR region at 3260cm^{-1}, 1620cm^{-1} , 1687cm^{-1} and may be assigned to $\nu_{N-H,}$ $\nu_{C=N,}$ ν_{-CONH} respectively. Disappearance of a pair of bands corresponding to (ν_{NH2}) stretch at 3400 & 3250 $cm^{-1}$and 1674cm^{-1} $(\nu_{C=O})_{PHQ}$ while appearance of a strong band at 1620 cm^{-1} indicates the condensation between both of the molecules [34-35].

The band corresponding to $\nu_{C=N}$ appears at lower frequency by 10-30 cm^{-1} in the complexes and indicates the coordination of nitrogen atoms of azomethine groups to metal atom [36] as a result of lower electron density around nitrogen atom of C=N bond.

Peak corresponding to $\nu_{C=O}$ group of the -CONH moiety has been shifted to lower side and appears around 1620–1640 cm^{-1} in the spectra of all the complexes[37] suggesting the involvement of oxygen of the carbonyl group in coordination with metal and drift of electron density from oxygen of >C=O to the metal ion. Shifting of C=N and C=O band of dihydrazide confirms the tetradentate coordination of ligand to metal.

Other bands present in the range 1300-1000 cm^{-1} in all the complexes may be assigned to (C-N) stretch [38].

In nitrate complexes, absorption bands are observed at 1430-1410, 1315-1280 and 1050-1017 cm^{-1} frequency suggests unidentate coordination of both nitrate groups to central metal ion [39].

Two specific bands corresponding to $(\nu_{C=O})_{acetate}$ and $(\nu_{C-O})_{acetate}$ are appeared in the region 1670-1650 cm^{-1} and 1290-1250 cm^{-1} respectively in all acetate complexes. The difference of around 380-390 between these two peaks indicates the unidentate coordination of the acetate ion with the central metal ion [40].

The bands appeared in the region 450-420 cm^{-1} are attributed to (M-N) vibrations and indicate the coordination of azomethine nitrogen to metal [41].

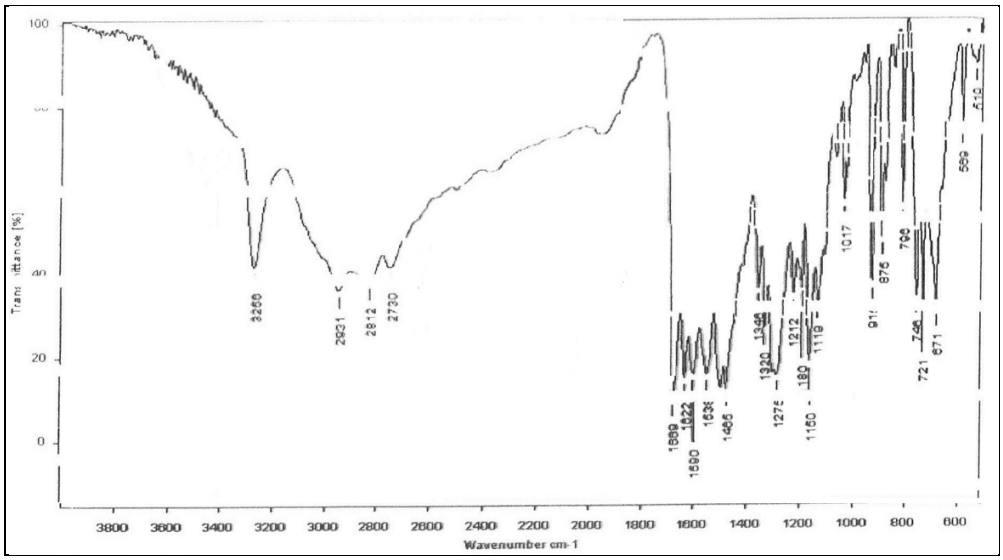


Fig.1 FT-IR spectrum of **$[Cr(L)(OAc)_2]OAc$ (compound 2) recorded at room temperature in the range 600-4000cm^{-1}**

3.3 *UV-VIS Spectral analysis and magnetic measurement*

Electronic spectral technique is very helpful to evaluate the results obtained from other techniques of structural investigation. The electronic absorption spectra of ligand and all complexes were recorded in DMSO at room temperature ranging 200nm-900nm. Broad peaks are observed near 27000cm^{-1}-29000cm^{-1} and 35000-36000cm^{-1}region in ligand which are assigned to intra ligand transitions of >C=O and C=N bond in the molecule. This band is observed slightly lower side in the complexes due to coordination of oxygen atom of >C=O and nitrogen atom of C=N bond and with metal ion and known as charge transfer band. [42]

Chromium complexes Magnetic moment of chromium complexes was observed between 3.9 - 4.50 B.M. at room temperature which is in proximity to the predicted values for three unpaired electrons in the metal ion [31]. The electronic spectra of Cr (III) complexes show bands at 22252 and 18234 cm-1 may be assigned to 4A2g → 4T2g (F) and 4A2g → 4T2g (P) respectively and pointing towards octahedral geometry[43].

Iron Complexes
The magnetic moment of iron complexes lie between 5.85-5.90 B.M. corresponding to the five unpaired electrons and is close to predicted high spin values for these metal ions. The electronic spectra of Fe (III) complexes show various bands at 13530, 18968, and 31518 cm-1 may be assigned to 6A1g → 4T1 (4D), 6A1g → 4T1g and 6A1g → 4T2g, respectively and pointing towards octahedral geometry[44].

3.5 ^{1}H NMR spectrum for macrocyclic complex [Cr (L)$(NO_3)_2$]NO_3 in DMSO-d_6 ,60MHz frequency at room temperature.

Peaks corresponding to –NH of hydrazide moiety, Ar-H of both the molecules were observed in the ^{1}H NMR spectrum of the ligand and complexes. A downfield shift of the peak for -NH proton is observed in complexes compared to the ligand due to the coordination with metal ion and decreased intensity of electrons around –NH proton.

3.6 Thermal analysis (TGA)
The TGA spectrum of compound 5 **[Fe (L)$(OAc)_2$]OAc** was recorded at temperature from 50^0C to 750^0C at a heating rate of 10^0C/min. and observed that decomposition starts at 300^0C (12.02%) which may be due to the removal of two chloride ions from the complex as the calculated value is 11.9% which resembles to the mass % loss in spectra. Decomposition temperature beyond 100^0C rules out the presence of coordinated water in the molecule. A sharp weight loss of 70.886% between 420^0C and 715^0C in TGA curve may be due to the decomposition of the organic part (ligand) from the compounds which is in accordance with the calculated value. Further horizontal constant curve is attributed to the presence of metal oxides residue as the remaining part [45] as the observed value (22%) resembles with the calculated value of corresponding metal oxide Fe_2O_3.

3.7 Biological results
3.7.1 Determination of bacterial susceptibility
For the detection of MIC the macro dilution broth method was performed. Serial dilutions of all test compounds ranging 512-16 µg /ml in DMSO were prepared within sterile tubes. Test compound containing tubes were inoculated with a standardized bacterial suspension of all strains with 10^7 cfu mL^{-1} concentration. DMSO was used as negative control. Tubes were incubated for 24 hrs and MIC for all test compounds and standard antibiotic was observed. (Table 2)

All experiments were performed in triplets and an average value is reported.

Table 2: In vitro ANTIBACTERIAL ACTIVITY OF synthesized species through agar well diffusion method

Compound.	Corresponding effect on given microorganism in terms of diameter of Zone of Inhibition in mm				**MIC(µg/ml)**			
	Staphylococcus aureus	***Bacillus cereus***	***Salmonella typhi***	***E.Coli***	***Staphylococcus aureus***	***Bacillus cereus***	***Salmonella typhi***	***E.Coli***
1.	12.4	12.6	13.2	2.0	128	128	128	256
2	16.3	16.2	14	2.2	32	64	64	128
3.	17.2	19.4	17.2	4	32	16	16	128
4.	16.4	19.5	17.4	-	32	16	32	-
5.	12.5	12.5	11.2	2	64	64	64	256
6.	14.5	17.6	14.4	2	64	64	64	256
Cipro	24	27.8	22.4	22	8	8	16	16
DMSO	-	-	-		-	-	-	-

(-) means no activity, Bacillus cereus, Staphylococcus aureus, Escherichia coli , Salmonella typhi. Here compound1= $C_{22}H_{14}N_4O_2$; compound 2 = [Cr(L)$(OAc)_2$]OAc ; compound 3=[Cr(L)$(NO_3)_2$]NO_3 ; compound4=[Cr(L)$(Cl)_2$]Cl compound 5=[Fe(L)$(OAc)_2$]OAc ; compound6= [Fe(L)$(NO_3)_2$]NO_3;

Fig. 2 : Zone of inhibition for compound 5 against Bacillus cereus

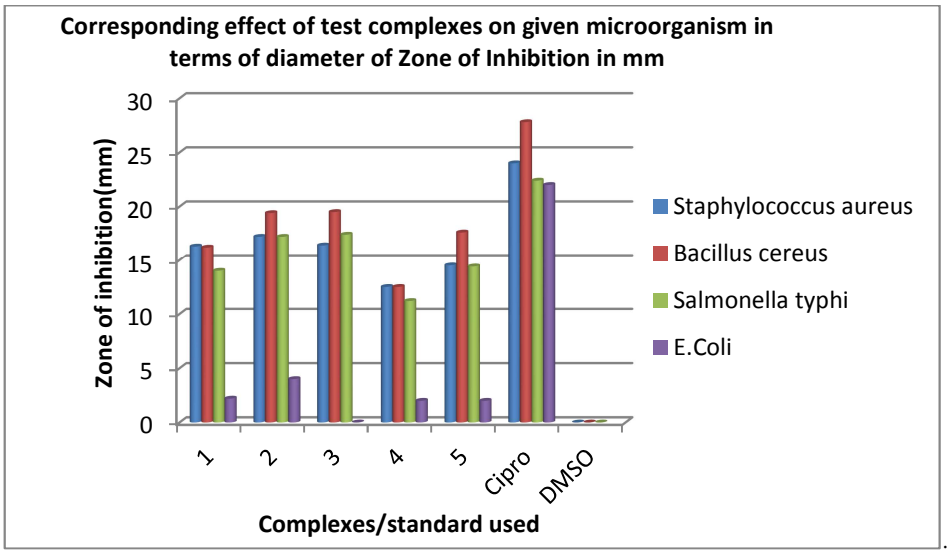


Fig.3: Comparative study of zone of inhibition for bacterial growth with standard antibiotic Ciprofloxacin

It was observed that all the compounds are more effective against gram +ve bacteria than gram –ve bacteria similar to the results reported earlier in literature [46-47]. None of the complexes are effective significantly against E.Coli. Complexes of Cr(III) are more effective than Fe(III) complexes against all the bacterial strains. Complexes were showing greater susceptibility to bacteria than the respective ligand similar to the results earlier reported in literature[54] and indicates the enhancement of lipophilic nature of ligand and better penetration of bacterial cell wall(bacterial susceptibility) on coordination. Compounds of Cr (III) are most effective against all the strains. It indicates that the effect of individual metal, its electron density, coordination potential, dipole moment, conductance also affect its overall biological behavior [48-49].

The antimicrobial results of the ligand exhibited a considerable enhancement on coordination with the transition metal ions against all bacterial strains.

3.7.2Antioxidant activity

It was observed that the absorbance of all test compounds has been significantly reduced significantly in comparison to pure DPPH solution (no test compound) (Table 3), which reveals the antioxidant nature of the complexes. All tests were performed thrice and an average value is reported. DMF was used as a negative control and DPPH was used as positive control.

Radical scavenging activity was calculated using the following formula:

% Radical scavenging activity= [O.D. $_{control}$ – O.D. $_{sample}$/ optical density $_{control}$]×100
Here OD= Optical density

Table 3: Absorbance of complexes and standard Ascorbic acid at different concentration at 517 nm

	Absorbance of test compounds at 517nm at different concentrations				
Concentration(µg/lt)	0.0	50.0	100.0	250.0	500.0
A $_{Ascorbic\ acid}$	1.245	0.843	0.657	0.315	0.145
A $_{Cr\ complex}$	1.245	0.754	0.673	0.385	0.256
A $_{Fe\ complex}$	1.245	0.498	0.498	0.422	0.345

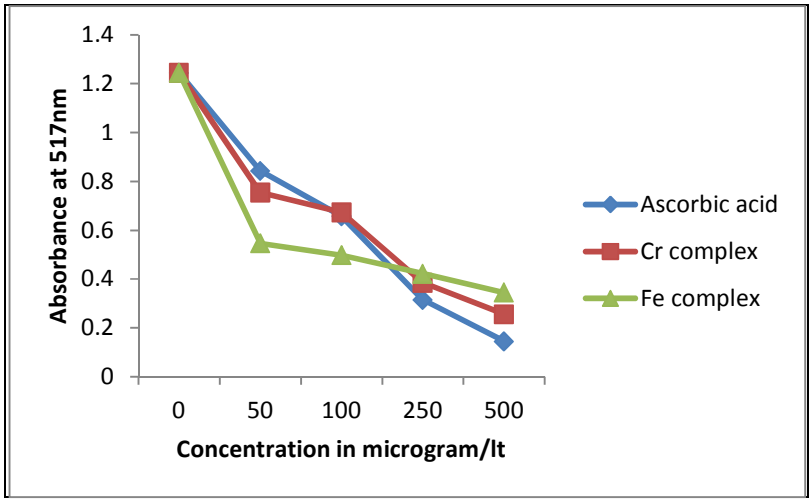


Fig.4: Comparative study of antioxidant activity of different test compounds with Ascorbic acid (standard)

All compounds showed significant free radical scavenging action through release of free radicals at different concentration and indicated that their antioxidant potential is increasing as the concentration of test compound increasing from 50µg/ml to 200µg/ml range. Complexes were most effective among all the complexes. Fe(III) complexes have given better results than the corresponding Cr(III) complexes may be due to the difference of number of unpaired electrons and its magnetic moment. Nitrate complexes are more effective than acetate complexes may be due to higher electron withdrawing effect of nitrate group than others which facilitates the easy release of proton and hence higher radical scavenging activity [50-51].

CONCLUSION

Present investigation shows that the tetradentate ligand derived from template condensation of 1,3-dicarbonyl-phenyl-dihydrazide and 9,10-phenanthrenequinone coordinates readily with all trivalent metal salts and afford the synthesis of octahedral complexes.

However detailed spectroscopic study including UV, IR, Mass and NMR was needed to investigate the influence of structure and coordination on the reactivity of the corresponding ligand.

Mass spectral study confirms a monocentric complex, while thermal studies have shown a good thermal stability of complexes. An investigation of biological behavior of all synthesized species has shown significant antibacterial and antiradical results.

A detailed structural and biological investigation of this series of complexes would throw more light on the influence of metal coordination on the reactivity of macrocyclic molecules which may be further explored and used as alternative therapeutic agents.

Abbreviations:
B.M.: Bohr magneton; DMF: N, N-dimethylformamide; DMSO: Dimethylsulphoxide; CFU: Colony forming unit; MIC: Minimum inhibitory concentration; MTCC: Microbial type culture collection; IR: Infrared; EDTA: Ethylenediaminetetraacetic acid; DPPH: 2,2-diphenyl-1-picrylhydrazyl 1,1-diphenyl-2-picrylhydrazyl

REFERENCES

[1] Rathi P. , Singh D.P., *Spectrochimica Acta Part A: Molecular and Biomolecular Spetroscopy,* **2015**; 136 : 381–387
[2] H. Zhou, C.; Wang, Y. ,*Current Medicinal Chemistry*, **2012**,19(2):239-280
[3]Chandra S. , Jain D. , Sharma A. K. ,Sharma P. , *Molecules* **2009**; 14(1): 174-190
[4] Firdaus F. , Fatma K., Azam M., Khan S.N., *Spectrochimica Acta Part A* **2009**;72(3): 591–596
[5] Shakir M., Varkey S.P., *Polyhedron* **1995**; Vol. 14(9): 1117-1127
[6] Singh D.P., Kumar K., Sharma C., *Eur. J. Med. Chem.***2009***;* 44: 3299-3304.
[7] Kumar G., Kumar D., Devi S., Johari R., Singh C.P., Eur. J. Med. Chem.**2010** 45(7): 3056-3062.
[8] Kulkarni A., Patil S.A., Badami P.S., Eur. J. Med. Chem **2009**; 44: 2904-2912.
[9] Bagihalli G.B., Avaji P.G., Patil S.A., Badami P.S., Eur. J. Med. Chem.**2008***;* 43: 2639-2649**.**
[10]Singh K., Bharwa M.S., Tyagi P., *Eur. J. Med. Chem.***2007**; 42(3): 394-402.
[11] Ramesh R., Maheswaran S., *J. Inorg. Biochem.***2003**; 96 : 457-462
[12]Shakir M., Khatoon S., Parveen S., Azim Y., *Transit. Met. Chem.***2007** 32(1) : 42–46.
[13] Andrei K. Yudin, *Chemical Science;* **2015**(1):1-844
[14] Chandra S., Pundir M., *Spectrochim. Acta A.***2008**; 69 (1): 1–7.
[15]Chandra S., Gupta L.K. , *Spectrochimica Acta Part A.***2005**; 62 4-5): 1089–1094.
[16] Chandra S., Gupta L.K., Agrawal S., *Transit. Met. Chem.***2007**; 32(2):558–563.
[17]Singh D.P., Kumar R., Malik V., Tyagi P., *J. Enz, Inhib. Med. Chem.***2007**; 22 (2):177–182
[18] Singh D.P., Kumar K., Sharma C., *Spectrochimica Acta Part A* .**2010**;75: 98–105
[19]Kumar G. , Devi S. , Johari R. , Kumar D. ,*European Journal of Medicinal Chemistry*,**2012**; 52 : 269-274
[20]Niasari M.S.,Daver F., *Inorg. Chem. Commun*. **2006** ;9 : 175–179.
[21] Prasad R. N., Gupta S., Jangir S., *J. Indian Chem. Soc.***2007**; 84 : 1191–1194
[22]Vanco J.,Marek J., Travnicek Z., Racanska E., Muselik J., Svajlenova O., *J. Inorg .Biochem.***2008**; 102:595-605
[23] Singh D.P., Kumar K., Mehani R., *Spectrochimica Acta Part A.***2011**; 78: 629–634
[24]Kucukguzel S.G, Rollas S., Kucukguzel I., Kiraz M., *Eur.J. Med. Chem*. **1999**;34(12) 1093-1100.
[25]Zhang S., Sherry A.D, *J. Solid State Chem.***2003**; 171(1-2): 38-43.
[26]Yang Z.Y., *Inorg. Met.-Org. Chem*.**2000**; 30: 1265-1272.
[27]Prasad R. N, Mathur M., Upadhyay A., *J. Indian Chem. Soc.***2007**; 84(12): 1202-1204
[28] Khan T.A., Rather M.A., Jahan N., Varkey S.P., Shakir M., *Transition Met. Chem*.**1998**; 23 (3): 283-285.
[29]Nagar R., *J. Inorg. Biochem*. 40 (**1990**) 349-356.
[30]Andrews J.M., *J. Antimicrob. Chemother.***2001**; 48: 5-16.
[31] Jorgensen J, Turnidge J., *Manual of Clinical Microbiology, Eleventh Edition.* ASM Press, Washington chapter **2015**; 71: 1253-1273.
[32]Tsai K., Hsu T.G., Hsu K.M., Cheng H., Liu T.Y., Hsu C.F., Kong C.W., *Free Radic.Biol. Med*.**2001**; 31: 1465-1472.
[33]Geary W.J., *Coord. Chem. Rev*.**1971**; 7 : 81–122.
[34] Singh A.K., Panwar A., Singh R., Beniwal S., *Transition Met. Chem.***2003**; 28 (2): 160-162
[35]Mruthyunjayaswamy B.H.M., Omkar B. I.,Jadegoud Y., *J. Braz. Chem.Soc.***2005**; 16 : 783.
[36]Pavia D.L., Lampman G.M., Kriz G.S., "Introduction to Spectroscopy" *New York, Harcourt College Publishers,* **2001**.
[37]Nishat N., Rahis-ud-din, Haq M.M., Siddiqi K.S., *Transition Met. Chem.* **2003**;28(8): 948-953.
[38]Singh D.P., Kumar R. and Tyagi P., *Transition Met. Chem.*,**2006**; 31(7): 970-973.
[39]Jouad E.M., Allain M., Khan M.A., Bouet G.M., *Polyhedron.***2005**; 24(2): 32
[40]Srivastava S., Kalam A., Synth. React , *Inorg. Met. Org. Chem*.**2004**; 34 : 1529.
[41]Cotton F.A., Wilkinson G., Murillo C.A., Bochmann M., *"Advanced Inorganic Chemistry", 6th ed., Wiley-Interscience, New York,* **1999**
[42]Nakamoto K., "Infrared & Raman Spectra of Inorganic & Coordination Compounds Part-B", *5th edition, Wiley Interscience Publication,* **1997**.
[43]Catterick J., Thornton P., *J. Chem. Soc., Dalton Trans*. **1975**;(3): 233-238.
[44]Singh D.P., Kumar K., Dhiman S.S., Sharma J., *J. Enzyme Inhib. Med. Chem*.**2009**; 24 : 795–803

[45]Khan T.A.,Naseem S., Khan S.N., Khan A.U., Shakir M., *Spectrochim. Acta part A.***2009**: 73: 622–629.
[46]Shankarwar S.G., Nagolkar B.B., Shelke V.A., Chondhekar T.K., *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy* **2015**;145 :188–193
[47]Kavitha P., Saritha M., Reddy K.L., *Spectrochim. Acta Part A Mol. Biomol. Spectrosc*.**2013**; 102 : 159–168.
[48]Chohan Z.H., Scozzafava A., Supuran C.T., *J. Enz. Inhib. Med. Chem.***2002;** 17 (4): 261–266
[49]Lessa J.A., Reis D.C., Da Silva J.G., Paradizzi L.T., Da Silva N.F., Fatima M.D.Carvalho A., Siqueira S.A.,Beraldo H., *Chem. Biodivers.*2012; 9 : **1955**-1966.
[50] Bolla J.M., Alibert-Franco S., Handzlik J., Chevalier J., Mahamoud A., Boyer G., Kiec-Kononowicz K., J.-M. Pages, *FEBS Lett*.**2011**; 585: 1682-1690
[51]Chohan Z.H., Pervez H., Rauf A., Khan K.M., Supuran C.T., *J. Enz. Inhib. Med.Chem.* **2004**; 19 : 417–423.