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# Synthesis and characterization of some transition metal complexes of norfloxacin in presence of 1,10-phenenthroline

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**ABSTRACT**

*Five new octahedral transition metal complexes of norfloxacin with Mn(II), Cd(II), Co(II), Zn(II) and Cr(III) metal ion have been synthesized hydrothermally in presence of a nitrogen containing heterocyclic compound 1,10-phenantroline. The complex were characterized with FT-IR, C H N analysis, UV–visible spectroscopy. Spectral studies suggest that the norfloxacin acts as a deprotonated bidentate ligand. Thermal studies were also carried out.*

**Keywords**: Synthesis, Fluoroquinolone, Norfloxacin, FT-IR, TGA

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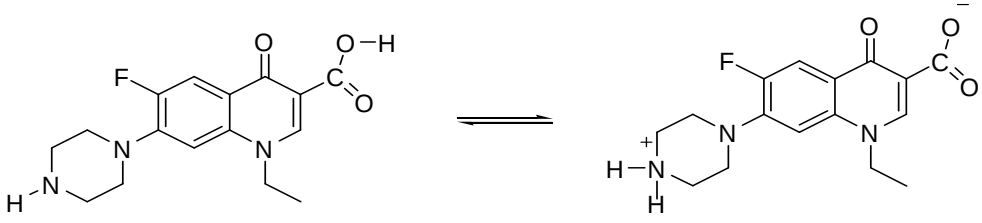
## INTRODUCTION

The study of interaction between quinolone and metals is an active area of research in bioinorganic chemistry [1-4]. Quinolones are the member of broad spectrum synthetic antibacterial agent containing 4-oxo-3-carboxylic-1,4-dihydroquinoline skeleton [5]. Quinolones are structurally related to nalidixic acid, a group of synthetic anti-bacterial agents [6]. A large number of structural modifications of nalidixic acid and related quinolones have been done based on structure activity relationships (SARS) [7]. It was found that the presence of fluorine atom at position 6 and a piperazine ring at position 7 without the presence of N at position 8 enhances the biological activity spectrum. The quinolones with these modifications are grouped together as fluoroquinolones [2]. They are employed as a drug in various infectious diseases like urinary tract infections, soft tissues infections, respiratory infections, bone joint infections, sexually transmitted disease, community acquire pneumonia, acute bronchitis, and sinusitis [1, 8]. Norfloxacin (nor) (Scheme 1) is the first member of the fluoroquinolones. These quinolone usually acts as bidented ligand due to the presence of ring carbonyl group at position-4 and one of the oxygen atoms of the carboxylic group at position-3 [9]. It has also been found that metal complex of quinolones show more bioactivity compared to the free



Norfloxacin  Zwitterionic form of Norfloxacin

**Scheme1 Molecular structure of nor and its zwitterion**

drug [10, 11]. All the quinolones can bind with the metal ions, only they differ in the extent of interaction from metal to metal [12]. In the literature different metal complex of norfloxacin were synthesised. These are

$[Mn(nor)_2](OAc)_2.8H_2O$, $[Fe(nor)_3]Cl_3.12H_2O$ and $[Co(nor)_2]SO_4.8H_2O$[13], $[ZrO(H_2O)(nor)_2].3H_2O$, $[MoO_2(nor)_2]$ and $[WO_2(nor)_2]$ [14] $[ZrO(nor)_2Cl\}.15H_2O$ and $[UO_2(nor)_3](NO_3)_2.4H_2O$ [15] $[Ag_2(nor)_2](NO_3)_2$, $[Cu(nor)_2(H_2O)_2]SO_4.5H_2O$ and $[Au(nor)_2(H_2O)_2]Cl_3$[16]. $[Th(nor)_2Cl_4]$, $[Zr(nor)_2Cl_2]Cl_2$ and$[Vo(nor)_2]SO_4$[17], $[Ti(nor)Cl_4]$, $[Cr_2(nor)_2(CO_3)_2(H_2O)_4]$, $[Cr(nor)_2Cl_2]Cl.{}_3H_2O$, $[Cr(nor)_2(OAc)_2]OAc.2H_2O$, $[Cr_2(nor)_2(SO_4)_2(H_2O)_4]SO_4$, $[Mn(nor)_2(H_2O)_2]$, $[Mn(nor)_2Cl_2]$, $[Mn(nor)_2(OAc)_2$, $[Ni(nor)_2SO_4]$ and $[Ni(nor)_2(OAc)_2$[18], $[Co(nor)_2(H_2O)_2](NO_3)_2$, $[Zn(nor)_2Cl_4].2H_2O$, $[Cd(nor)_2]Cl_4.3H_2O$, $[Hg(nor)_2Cl_4].2H_2O$ and $[Hg(nor)_3Cl_4]$[19] $[Fe(nor)(H_2O)_4](ClO_4).5H_2O$, $[Fe(nor)_2(H_2O)_2](ClO_4)_2.6H_2O$, $[Fe(nor)_3(H_2O](ClO_4)_2.8H_2O$, $[Fe(nor)_4](ClO_4)_2.10$ $H_2O$, $[Fe(nor)(H_2O)_4](ClO_4)_3.6H_2O$, $[Fe(nor)_2(H_2O)_2](ClO_4)_3.5H_2O$, $[Fe(nor)_3(H_2O)](ClO_4)_3.6H_2O$ and $[Fe(nor)_4](ClO_4)_3.$ $10H_2O$[20] $[Cu(pph_3)_2(nor)]$ $ClO_4$ [21], $[Ag(nor)_2NO_3]$[22] $[W(nor)(H_2O)(CO)_3](nor).H_2O$ [23]. In the present work we have synthesised a five new transition metal complex of norfloxacin with Mn(II), Cd(II), Co(II), Zn(II) and Cr(III) metal ion in presence of nitrogen containing heterocyclic ligand 1,10-phenanthroline (phen) hydrothermally by gradual heating and cooling.

## MATERIALS AND METHODS

### *2.1 Materials*

Norfloxacin has been purchased from Sigma Aldrich. Phenanthroline and the metal salts were obtained from Merck. All the chemicals used for this work were of analytical grade.

### *2.2 Synthesis of the complex*

An equimolar mixture of metal chloride and phenanthroline in 15 ml of 1:1 solvent mixture of methanol and acetone was stirred for 10 minutes on a magnetic stirrer at room temperature. Then 5 ml equimolar solution of norfloxacin in the same solvent mixture was added drop by drop under stirring condition. Further, the resulting mixture was heated in a hydrothermal vessel in programmed temperature oven at 100°C for 24 hrs. Then it was gradually cooled up to room temperature after 72 hrs (Scheme 2), leading to coloured powder complex.

### *2.3 Physical measurements*

Infra-red spectra were recorded on a spectrometer Perkin Elmer Spectrum BXII in the range of 400-4000 $cm^{-1}$ by preparing sample pallets with KBR. UV-Visible spectra were recorded in DMSO at concentration 10 ppm on an instrument Analytik jena SPECORD 250 in the range of 250-900 nm. C, H and N elemental analysis were performed on the instrument named elementer vario ELIII. TGA measurements were carried out in a nitrogen atmosphere from ambient temperature to 900°C using Perkin Elmer Diamond.

**Table1. Molecular weight, yield, colour, elemental analysis of the nor and its complexes**

| Entry | Mol.Wt | Yield (%) | Color | Elemental Analysis (%) | | |
|---|---|---|---|---|---|---|
| | | | | C | H | N |
| **a** | 334.36 | - | white | (61.07)<br>61.42 | (6.33)<br>6.76 | (12.57)<br>12.11 |
| **b** | 759.55 | 65 | yellow | (49.02)<br>48.81 | (4.23)<br>4.35 | (9.22)<br>9.44 |
| **c** | 823.99 | 82 | white | (42.27)<br>42.30 | (3.26)<br>3.5 | (8.59)<br>8.39 |
| **d** | 716.47 | 89 | gray | (48.61)<br>48.33 | (6.21)<br>6.02 | (9.77)<br>10.19 |
| **e** | 764.10 | 76 | white | (51.47)<br>51.62 | (5.33)<br>4.99 | (9.39)<br>9.85 |
| **f** | 708.96 | 83 | green | (49.13)<br>49.55 | (5.39)<br>5.02 | (9.89)<br>10.14 |

## RESULTS AND DISCUSSION

### 3.1 FT-IR

FT-IR band assignments of the synthesised complexes were done by comparing the spectra of the complexes with those of the free ligand nor to determine the mode of coordination of the ligand. Table2 gives the comparison for the band assignments between synthesised complexes and free ligand. FT-IR spectra of free ligand in KBr disk shows the ketonic stretch $\nu(C=O)_{keto}$ at 1617 $cm^{-1}$ which is slightly shifted to the range of 1618-1627 $cm^{-1}$ in the synthesised complexes due to chelation. In the free ligand characteristic absorption band at ~1733 $cm^{-1}$ for the $\nu(C=O)_{carb}$ vibration of the carboxylic group is observed and this band is replaced in the newly synthesised complexes by the two characteristic bands in the range of 1555-1581 $cm^{-1}$ and 1340-1386 $cm^{-1}$ for asymmetric and symmetric stretching vibration of carboxylate group respectively [24]. This indicates the involvement of the keto and carboxylic group in the coordination with metal ions (Fig.1). According to Deacon and Phillips [25] when the

Δν (where Δν = $\nu(O\text{-}C\text{-}O)_{as}$–$\nu(O\text{-}C\text{-}O)_s$) value is ~ 200 $cm^{-1}$ then carboxylate group interacts with metal ion in monodentate way. Δν of the synthesised complexes is found in the range of 195-237$cm^{-1}$ that indicates the monodentate interaction of the carboxylate group with metal ion. The FT-IR data of the complex shows a very strong and broad band at 3368 $cm^{-1}$ and medium to weak bands at 2841 and 2487 $cm^{-1}$. These two bands confirm the vibration of quarternized nitrogen of the piperazinyl group indicating the zwitterionic form of free nor involves during coordination with the metal ions.

**Table 2. Characteristic FT-IR assignments ($cm^{-1}$) of nor and the complexes**

| Entry | $\nu(C=O)_{keto}$ ($cm^{-1}$) | $\nu(O\text{-}C\text{-}O)_{as}$ ($cm^{-1}$) | $\nu(O\text{-}C\text{-}O)_s$ ($cm^{-1}$) | Δν ($cm^{-1}$) |
|---|---|---|---|---|
| a | 1617 | 1733 | - | - |
| b | 1623 | 1577 | 1340 | 237 |
| c | 1618 | 1583 | 1349 | 234 |
| d | 1626 | 1555 | 1349 | 206 |
| e | 1623 | 1581 | 1386 | 195 |
| f | 1627 | 1560 | 1354 | 206 |

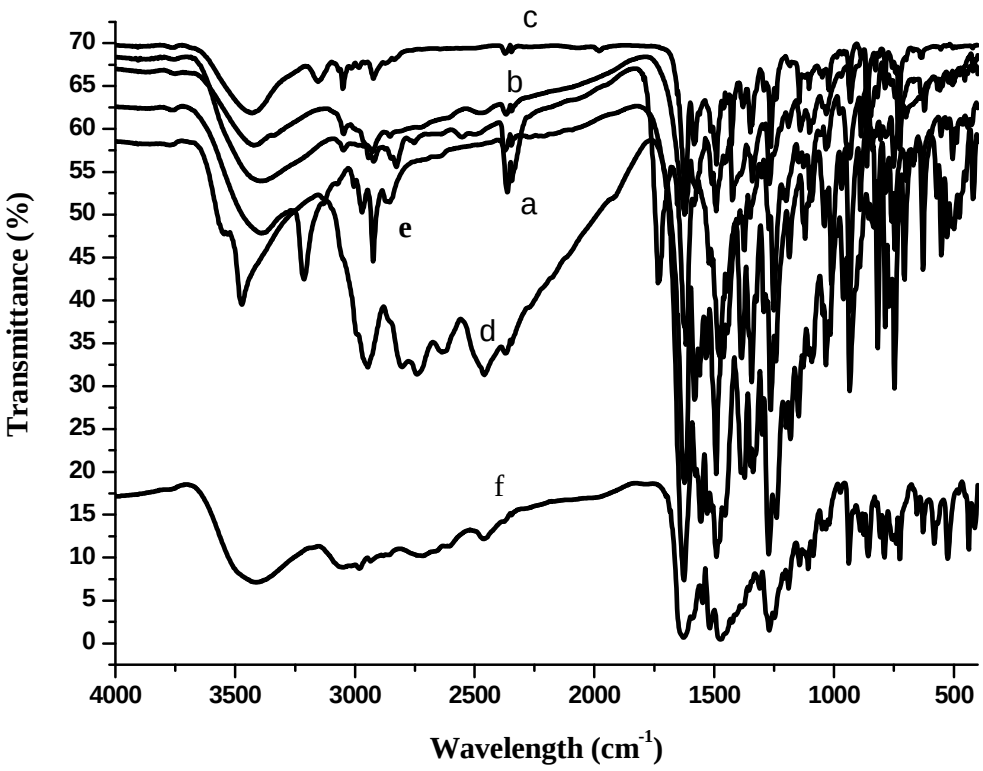



**Fig.1 Ft-IR bands of a.Nor b.[Mn(Nor)(phen)Cl $H_2O$]Cl.$CH_3OH$ c. [Cd(Nor)(phen)$(H_2O)_2$]$Cl_2$.5$H_2O$ d.[Co(Nor)(Phen)$(H_2O)_2$]$Cl_2$2$H_2O$ e. [Zn(Nor)(Phen)(OAC)]OAC4$H_2O$ f. [Cr(Nor)(phen)$Cl_2$]Cl,2$H_2O$**

### 3.3 Electronic spectra

Electronic spectra of the synthesized complex and the free ligand nor were studied in the range of 250-900 nm in DMSO. Two bands have been found at 285 nm and 335 nm in case of free ligand. These two bands assigned to $\pi - \pi^*$ and $n-\pi^*$ transitions respectively. These two transitions were observed due to the presence of aromatic ring containin keto group and the carboxylic group. Pattern of the electronic spectra of metal complexes is similar to that of the free ligand indicating that the ligand has not changed its structure in the complex. But these two spectra only differ in the absorbance. The band at 285 nm in the spectra of the complex is shifted hypochromically

compared to the free ligand suggesting that the keto and carboxylic group participate in the complex formation (Fig.2).

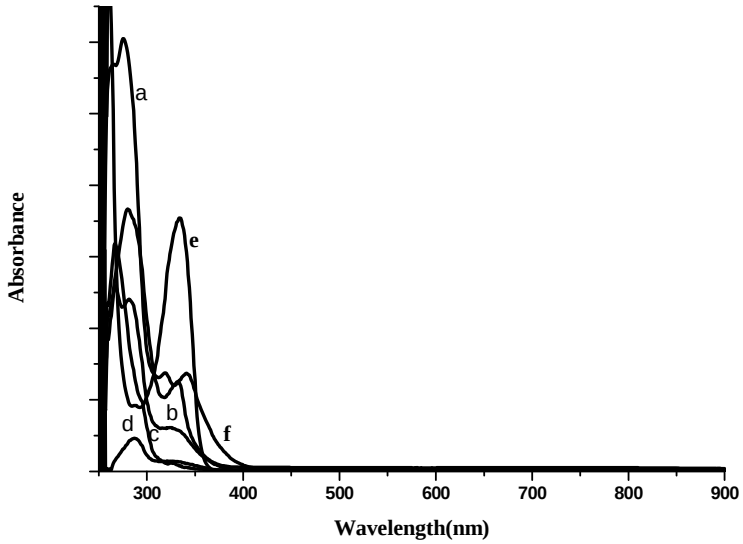



**Fig.2 Uv-vis plot of a. Nor b. [Mn(Nor)(phen)Cl $H_2O$]Cl.$CH_3OH$ c.[Cd(Nor)(phen)$(H_2O)_2$]$Cl_2$.$5H_2O$ d. [Co(Nor)(Phen)$(H_2O)_2$]$Cl_2 2H_2O$ e [Zn(Nor)(Phen)(OAC)]OAC$4H_2O$ f.[Cr(Nor)(phen)$Cl_2$]Cl,$2H_2O$**

### 3.4 Thermal analysis

Thermal analysis of the metal complexes were also studied starting from ambient temperature to 900°C with controlled heating rate of 10°C$min^{-1}$ under nitrogen atmosphere. The temperature ranges, percentage weight loss and eliminated moiety in ever decomposition has been listed in Table 3. In case of free ligand 3.12% of weight loss was observed in the temperature range of 31-256°C. Second step of weight loss started at 256°C and ended at 562°C with 67.29 % of weight loss and third decomposition occurs between 562°C and 731°C with a weight loss of 5.23%. Melting point of Nor is 221°C.

In case of Mn(II) metal complex first weight loss was observed in the temperature range 26-257°C with 14.84 % of weight loss. After that second step starts at 257°C and ends at 495°C with a mass loss of 47.37%. The third step was observed in the temperature range 495-901°C with weight loss of about 30.33%. Melting point of this complex is 244°C.

In case of Cd(II) metal complex first step of weight loss occurs in the temperature between 24°C and 278°C with 7.18% of weight loss. Then second step of weight loss was started at 278°C and ended at 378°C with the weight loss of 20.81%. The third step of weight loss was observed in the temperature range 378-509°C with 21.59% of weight loss. Then last step of weight loss was upto 895°C with 50.5% of weight loss. Melting point of this complex is 289°C.

In case of Co(II) metal complex first step of weight loss was observed in the temperature range 28-300°C with 8.21% of weight loss. The second step of weight loss was started at 300°C and continued up to 548°C with 41% of weight loss and the third step of weight loss was occurred at the temperature range 548-898°C with 30.14 % of weight loss. Melting point of this complex is 347°C.

First step of weight loss was observed in the temperature range 18-181°C in case Zn(II) metal complex with 7.29 % of weight loss. The second step of weight loss occurred between 181°C and 362°C with 52.55 % of weight loss. The third step of weight loss continued upto 898°C with 26 % of weight loss. Melting point of this complex is 311°C.

In case of Cr(III) metal complex first step of weight loss was observed at the temperature range 17-83°Cwith weight loss of 7.56%. In the second step 7.53 % of weight loss was observed in the second step of weight loss in the temperature range 83-333°C. In the last step 27.52 % of weight loss was observed in the temperature range 333-599°C. Melting point of this complex is 351°C.

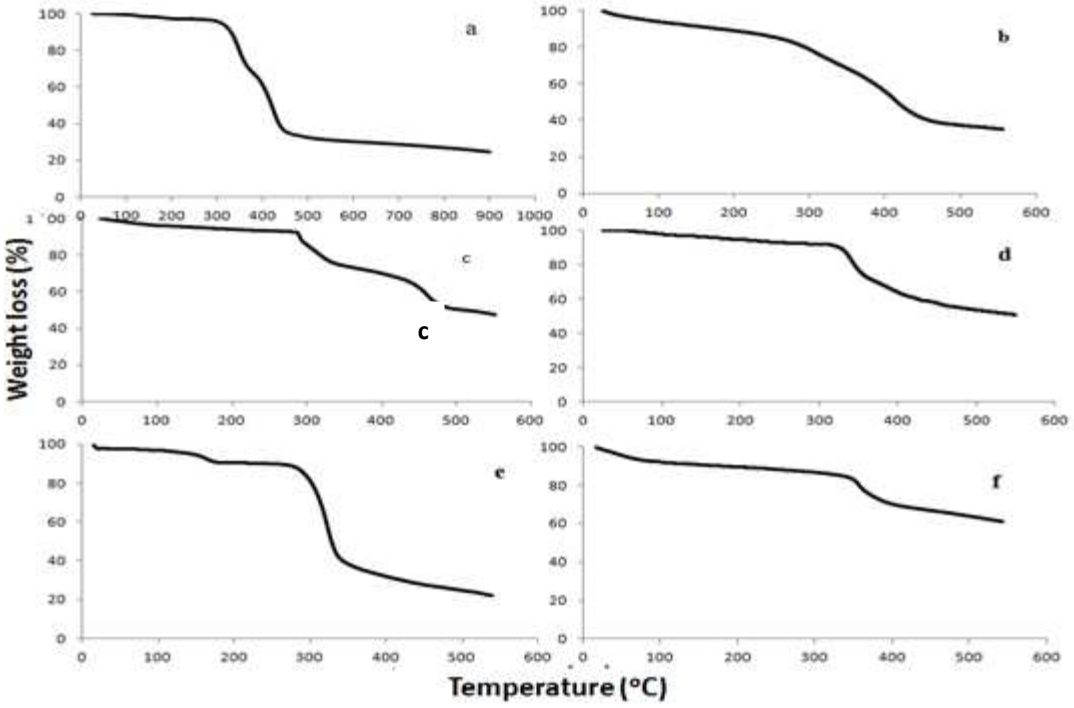



**Fig. 3 TGA plot of a. Nor b. [Mn(Nor)(phen)Cl $H_2O$]Cl.$CH_3OH$ c.[Cd(Nor)(phen)$(H_2O)_2$]$Cl_2$.5$H_2O$ d. [Co(Nor)(Phen)$(H_2O)_2$]$Cl_2$2$H_2O$ e [Zn(Nor)(Phen)(OAC)]OAC4$H_2O$ f.[Cr(Nor)(phen)$Cl_2$]Cl,2$H_2O$**

It has been also found that melting point of synthesised complex is more than that of parent quinolone. From the above thermal study it is obvious that synthesised complex is more thermally stable than its parent ligand Nor.

**Table 3 Data of the thermal analysis of nor and the complexes**

| Entry | Steps | Temp. range ($^o$C) | Weight loss (%) Found Calc | M.P (°C) | Eleminated moiety |
|---|---|---|---|---|---|
| a | 1st<br>2nd<br>3rd | 31-256<br>256-562<br>562-731 | 3.12 5.75<br>67.29 69.37<br>5.23 7.85 | 221 | $C_2H_4$<br>HF +4$C_2H_2$ +Co+$CO_2$+$N_2$<br>2$C_2H_5$ + 0.5$N_2$ + 0.5$H_2$ |
| b | 1st<br>2nd<br>3rd | 26-257<br>257-495<br>495-901 | 14.84 15.15<br>47.37 45.30<br>30.33 31.62 | 244 | 3$H_2O$+0.5$F_2$+0.5 $Cl_2$<br>Phen +$CO_2$+0.5$Cl_2$+$H_2O$<br>Piperazine ring+$CH_3$ |
| c | 1st<br>2nd<br>3rd<br>4rth | 24-278<br>278-378<br>378-509<br>509-895 | 7.18 6.67<br>20.81 20.26<br>21.59 21.68<br>50.50 46.39 | 289 | 2$H_2O$+0.5$F_2$<br>Piperazine ring 3$H_2O$ $CH_3$<br>5$C_2H_2$+$CO_2$+Phen+$N_2$ |
| d | 1st<br>2nd<br>3rd | 28-300<br>300-548<br>548-898 | 8.21 7.68<br>41.0 40.44<br>30.14 31.18 | 347 | 2$H_2O$+0.5$F_2$<br>2$H_2O$+Phen+0.5$Cl_2$+$CH_3$<br>Piperazine ring Cl |
| e | 1st<br>2nd<br>3rd | 18-181<br>181-362<br>362-898 | 7.29 7.15<br>52.55 53<br>26 25.74 | 311 | 2$H_2O$+0.5$F_2$<br>2$H_2O$+2OAC+Phen+$CO_2$<br>2$CH_3$+$C_2H_5$ |
| f | 1st<br>2nd<br>3rd | 17-83<br>83-333<br>333-599 | 7.56 7.75<br>7.53 6.71<br>27.52 23.76 | 361 | 2$H_2O$+0.5$F_2$<br>$CO_2$<br>Pyperazine ring |

## CONCLUSION

The synthesis and characterization of neutral binuclear mixed ligand metal complex of Nal and Phen with different metal ions have been realized with physicochemical and spectroscopic methods. The ligand is bonded to metal ion via the keto oxygen and one carboxylic oxygen.

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