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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF MANGANESE(II) AND NICKEL(II) COMPLEXES OF 7-DIETHYLAMINOBENZYL-8-HYDROXYQUINOLINE

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Abstract

8-Hydroxyqunoline Mannich base namely 7-diethylaminobenzyl-8-hydroxyqunioline(DEBQ) was synthesized and characterized by elemental analysis and spectral studies. Chelates of DEBQ with manganese(II) and nickel(II) were isolated and structurally characterized by elemental analysis, electrical conductance, magnetic susceptibility measurement, thermal analysis, IR,UV-Vis, EPR and Mass spectral data. The Mannich base ligand is bidentate and chelates through the phenolic oxygen and the aliphatic tertiary amino nitrogen atoms. Based on the magnetic and electronic spectral data all the Mn^{II} complexes are assigned an octahedral geometry and Ni^{II} complexes are assigned a tetrahedral geometry. Antimicrobial susceptibility screening of the Mannich base shows that it possesses excellent activity when compared to the standard drugs and the metal complexes studied. Among the chelates, Mn^{II} chelate is more potent than Ni^{II} chelate. Thermal analysis of a few compounds shows two stage decomposition patterns.

Keywords: 8-Hydroxyquinoline, Mannich base, Thermal decomposition, Antimicrobial screening, Metal chelates.

Introduction

Synthetic chemists and pharmacologists show much interest in heterocyclic compounds containing quinoline moiety because of their unique chemical and pharmacological properties (Balasubramanium M and Keay, JG, 1996; Micheal IP, 1997; Maguire M P et al, 1994).Quinoline derivatives exhibit versatile pharmacological properties(Vetrivel Nadaraj et al, 2006; Pandey V.K and Menal Tondan, 2001; Yuki Sowda et al., 2004; Brain D Lee et al 2004; Singh O MV and Muthukrishnan M, 2001; Guytan A C and Hall JE, 1998; Rao A et al, 2002; Meth-Cohn et al., 1981) such as anti-inflammatory, antibacterial, antifungal, antiallergic, antidepressant, antiasthmatic, antimalarial, antiviral, antitumour, neuroleptic, antihypertensive, cytotoxic, hypnotic, sedative,bronchodilator etc activities.8-Hydroxyquinoline is toxic if injected directly but its derivatives are useful as medicine in view of their biological activities . 8-Hydroxyquinoline is much useful in analytical chemistry also due to its chelating ability(Bassett J et al, 2000).When 8-hydroxyquinoline is subjected to Mannich condensation with aldehydes and secondary amines it yields Mannich bases which could display more potent pharmacological properties and also stronger chelating tendencies. Mannich base coordination chemistry has been a popular area of research due to the diverse range of biological, analytical and industrial applications of the Mannich base metal chelates (Sathya et al, 2012; Muthukumar C et al, 2012; Ramesh M and Sabastiyan A,2012, Sabastiyan A and Yosuva Suvaikin M,2012). Hence in this work, Mn^{II} and Ni^{II} chelates of 7-diethylaminobenzyl-8-hydroxyquinoline(DEBQ) have been synthesized, characterized and their antimicrobial potency screened against a few pathogenic micro-organisms.

Experimental

Materials and Methods

All the chemicals and solvents used were AR grade products. The microelemental analyses were performed using Carlo Erba 1108 CHN analyzer. Metals and anions were estimated by conventional wet chemical analyses. Molar conductivities were measured in ~ 10^{-3} M DMF solutions at room temperature using Systronics Conductivity Meter 304. FT-IR Spectral measurements were made with Perkin - Elmer Spectrum – 1 FT-IR Spectrometer as KBr pellets. Mass spectra were recorded using JEOL D-300 (EI) Mass Spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on JEOL GSX-400 FT NMR Spectrometer (400 MHz) employing TMS as internal reference and DMSO-d_6 as solvent. Electronic absorption spectra were measured in DMF solutions using Perkin - Elmer EZ301 Spectrophotometer. Magnetic susceptibility measurements were made on a Gouy magnetic balance at room temperature using $Hg[Co(SCN)_4]$ as calibrant. Simultaneous TG/DTA/DTG thermograms were recorded in the admosphere of air on a Perkin-Elmer Thermal analyzer.

Synthesis of 7-diethylaminobenzyl-8-hydroxyquinoline(DEBQ)

The Mannich base (DEBQ) was synthesized (Tromontini,1973; Tromontini M and Angiolini L,1994)by interacting 8-hydroxyquinoline(14.51g, 0.l mole) with benzaldehyde(10.6g, 0.1mole) and diethylamine (7.31g, 0.1 mole) in acetone medium at room temperature.The brownish-yellow solid compound formed was filtered and purified by recrystallization in ethanol (Yield ~ 70%, melting point : 63 – 64^0C). DEBQ is systematically named as 7-diethylamino(phenyl)methylquinolin-8-ol. The synthesis and characterization of this Mannich base has been already reported by us(Muthukumar C et al,2013).

Preparation of Mn^{II} and Ni^{II} complexes of DEBQ

The Mn^{II} and Ni^{II} complexes were isolated by interacting the respective hydrated metal salt (0.01 mole) with the ligand DEBQ(0.01mole) in hot ethanolic medium. The precipitated metal complexes were filtered, washed with ethanol and dried in a hot air oven at ~70^0C.

Invitro antimicrobial screening

Antimicrobial screening of the organic ligand and its metal complexes was carried out by agar well diffusion technique (Cruickshankt R,1975). *S.aureus* and *E.coli* were the bacterial strains and *P.Chrysogenum* and *A.niger* were the fungal species employed. The concentrations of test samples in DMSO solutions were 50 and 100 µg/mL. Antimicrobial activities of samples were determined by measuring the diameters of zones of inhibition (mm) in Muller Hinton agar medium after 24 hours of incubation for bacterial species and after 48 hours of incubation for fungal species. All the experiments were performed in triplicate. Growth inhibition produced by a particular sample was compared with that of the standard bacterial drug ampicillin and that of standard fungal drug amphotericin-B.

Results and discussion

Structural characterization of DEBQ

Elemental composition Calculated for $C_{2O}H_{22}N_2O$: C 78.43; H 7.189; N 9.15% Found C 78.44; H 7.20; N 9.16%. FT-IR absorption frequencies (cm^{-1} in KBr) : 3392 ν_{OH} ; 3049,3100 ν_{CH} ; 1579, 1471-1409 $\nu_{C=C}$ and $\nu_{C=N}$ aromatic ; 1379 $\nu_{CN\,;}$ 1093 ν_{CO}; 1284 – 1275 $\nu_{CNC\,.}$UV – Vis data (λ in nm, in DMF): 316 n- $\pi^*_;$ 260 π - π^*. . ^1H NMR chemical shifts (δ in ppm) : 7.2 – 8.2 pyridine ring protons; 6.9 – 7.2 benzene ring protons, 6.4 benzylic proton; 2.2 $N(CH_2)_2$ protons; 1.3 CH_3 protons, 6.6 OH proton. ^{13}C NMR chemical shifts (δ in ppm) : 137.6 ,127.6 bridgehead carbons in quinoline moiety; 126.3 -129.3 other aromatic carbons,71.3 benzylic carbon;45 $N(CH_2)_2$ carbons;148.1 carbon with OH group. Mass spectral data : molecular ion (m/z):306. The structural characteristics of DEBQ have been communicated by us(Muthukumar C et al,2013).

Based on these physico–chemical data, the structure of DEBQ is confirmed as given in Figure 1.

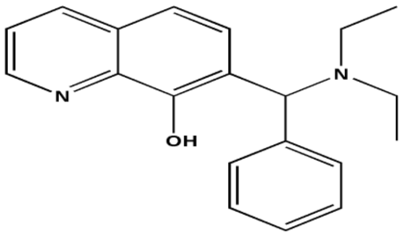

Figure 1 Chemical structure of DEBQ

Structural characterization of metal complexes

The analytical and conductivity data of the metal complexes of DEBQ are provided in Table1. These data indicate that the isolated metal complexes have 1:1 stoichiometry and are non-ionic in behaviour (Greay WJ, 1971). Further, the mass spectrum of the Ni^{II} sulphato complex(Fig.2) registers the molecular ion peak at 461,which indicates 1:1 stoichiometry for the same. The non-electrolytic behaviour of metal complexes suggests the bonding of anions to the respective metal ion in the complex species.

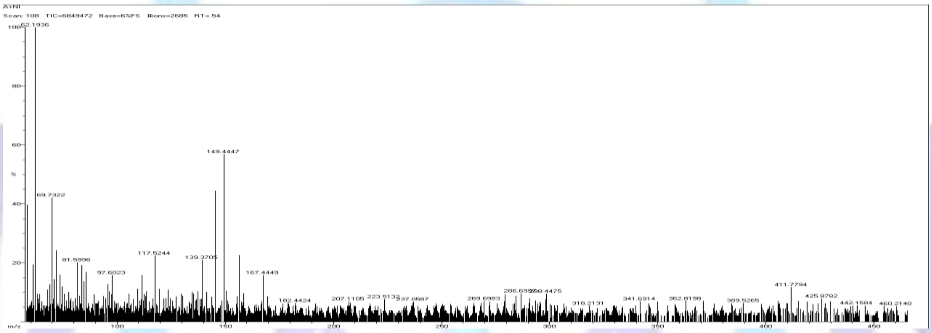

Figure 2 Mass Spectrum of $NiSO_4$.DEBQ

Compound	%C Found (Calc)	%H Found (Calc)	%N Found (Calc)	%Metal Found (Calc)	%Anion Found (calc)	λ_M $\Omega^{-1} cm^{-2} mol^{-1}$
DEBQ	78.44 (78.43)	7.20 (7.189)	9.16 (9.15)	-	-	-
$MnCl_2$.DEBQ	55.52 (55.57)	5.01 (5.09)	6.44 (6.48)	12.70 (12.72)	16.49 (16.41)	15
$Mn(NO_3)_2$.DEBQ	49.41 (49.49)	4.59 (4.53)	11.57 (11.54)	11.30 (11.32)	---- (25.57)	13
$MnSO_4$.DEBQ	52.59 (52.52)	4.80 (4.81)	6.17 (6.12)	12.00 (12.02)	21.00 (21.01)	24
$NiCl_2$.DEBQ	55.10 (55.09)	5.11 (5.05)	6.43 (6.42)	13.42 (13.47)	16.21 (16.27)	21
$Ni(NO_3)_2$.DEBQ	49.16 (49.11)	4.55 (4.50)	11.49 (11.45)	12.03 (12.01)	---- (25.37)	19
$NiSO_4$.DEBQ	52.04 (52.09)	4.70 (4.77)	6.01 (6.077)	12.72 (12.74)	20.89 (20.83)	09

Table 1 Analytical and molar conductance data for DEBQ and its metal complexes

Infrared spectral studies

The relevant IR absorption frequencies recorded for the ligand DEBQ and its metal complexes (Silverstein RM and Webster FX,1997; Nakamoto K,1978; Tamilvendan D et al,2010; Ferraro JR.1971) are provided in Table 2.A broad absorption at 3392cm^{-1} is attributed to the presence of a phenolic OH group in the quinoline moiety of the organic ligand. In the vibrational spectra of the Mn^{II} and Ni^{II} metal complexes, this band appears split and shifted to 3383-3326cm^{-1} region predicting the coordination of the phenolic oxygen atom to the metal ion. Normally when an aqueous solution of a 8-hydroxyquinoline derivative is added to an aqueous solution of the metal salt, the quinoline N and ionized phenolate O$^-$ chelate to the metal ion to precipitate the coordination compound. But in the precent study, the complex preparation was attempted in an ethanolic medium and the ionization of the phenolic OH in to O$^-$ was not possible.Also the presence of anionic groups such as Cl$^-$,NO$_3^-$ and SO$_4^{2-}$ in the complex species excludes the existence of phenolate anion in the coordination compounds. Further the pyridine ring vibrations which are usually observed at about 604cm^{-1} (inplane ring deformation) and 405cm^{-1} (out of plane ring deformation) have not shifted to high frequencies in the spectra of the complexes indicating non -involvement of the pyridine ring nitrogen atom in coordination

The ligand absorption bands observed at 1284-1275cm^{-1} are ascribed to the C-N-C stretching vibrations of the diethylamino moiety. But in the IR spectra of the metal complexes, these vibrations have shifted to a lower region of 1273-1208cm^{-1} pointing to the bonding of the aliphatic tertiary amino nitrogen atom to the metal ion. The coordination of a tertiary amino nitrogen is not sterically favourable, but the possibility of chelation tends to its coordination to a metal ion. Further the existence of new non-ligand bands in the regions 606-529cm^{-1} and 526-420cm^{-1} which indicate ν_{MO} and ν_{MN} vibrations respectively also predict the bidentate coordination of the Mannich base ligand through the phenolic OH group and the diethylamino nitrogen atoms. The nitrato groups in Mn^{II} complex exhibit vibrations at 1575(ν_5),1371(ν_1)and 1031cm^{-1} (ν_2). The very high separation between ν_1 and ν_5 peaks(204cm^{-1}) confirms the bidentate chelation of nitrato groups. But in the nickel(II) nitrato complex the corresponding vibrations are found at 1462,1384 and 1033cm^{-1}. The very low separation between ν_5 and ν_1(78cm^{-1}) confirms the unidentate behaviour of nitrato groups. The bidendate chelation behaviour of sulphato group in Mn^{II} and Ni^{II} sulphato complexes is also inferred from their IR absorption bands. In the Mn^{II} sulphato complex the absorptions observed at 1369,1159,1018cm^{-1}(ν_3); 825(ν_1); 652, 625, 606cm^{-1}(ν_4) and 526 cm^{-1}(ν_2) are indicative of bidentate sulphato coordination. In the Ni^{II} sulphato complex,the relevant absorptions are observed at1459,1389,1124 (ν_3);889(ν_1);718,618(ν_4)and 484cm^{-1}(ν_2) suggesting bidentate chelation of sulphato group with Ni^{II} ion.

Compound	ν_{OH}	$\nu_{C\text{-}N\text{-}C}$	$\nu_{C\text{-}O}$	$\nu_{M\text{-}O}$	$\nu_{M\text{-}N}$
DEBQ	3392	1284-1275	1093	-	-
MnCl$_2$.DEBQ	3326	1271-1237	1104	580	487
Mn(NO$_3$)$_2$.DEBQ	3372	1273-1226	1092	599	450
MnSO$_4$.DEBQ	3368	1272-1226	1103	606	526
NiCl$_2$.DEBQ	3356	1208	1100	550	471
Ni(NO$_3$)$_2$.DEBQ	3383	1209	1109	524	471
NiSO$_4$.DEBQ	3326	1225	1119	515	485

Table 2 IR Spectral data of DEBQ and its metal complexes (cm^{-1})

Magnetic and electronic spectral studies

The colours, magnetic moments and the electronic absorptions (Lever ABP,1968) of the Mn^{II} and Ni^{II} complexes are summarized in Table 3. Mn^{II} chloro, nitrato and sulphato complexes with DEBQ are coloured red brown indicating that they may be six coordinate octahedral complexes. Generally octahedral complexes of Mn^{II} ion exhibit electronic absorption bands which are attributed to three spin allowed transitions $^6A_{1g}\rightarrow{}^4T_{1g}(\nu_1)$, $^6A_{1g}\rightarrow{}^4A_{1g}+{}^4E_g(\nu_2)$ and $^6A_{1g}\rightarrow{}^4T_{2g}(\nu_3)$ respectively. In the present study, the Mn^{II} chloro, nitrato and sulphato complexes exhibit absorption bands at 13205, 12670 and 13150cm^{-1} respectively due to $^6A_{1g}\rightarrow{}^4T_{1g}(\nu_1)$ transition. They also exhibit absorptions at 22510, 22760 and 22480cm^{-1} respectively due to $^6A_{1g}\rightarrow{}^4A_{1g}+{}^4E_g(\nu_2)$ transition. Absorptions of the respective complexes observed at 25220, 25160 and 25380cm^{-1} are due to $^6A_{1g}\rightarrow{}^4T_{2g}(\nu_3)$ transition. The Mn^{II} chloro, nitrato and sulphato complexes of DEBQ record magnetic moment values at 5.18, 5.25 and 5.3B.M. respectively confirming the high spin octahedral geometry. The structures of these Mn^{II} complexes are shown in Figure 3a-c.

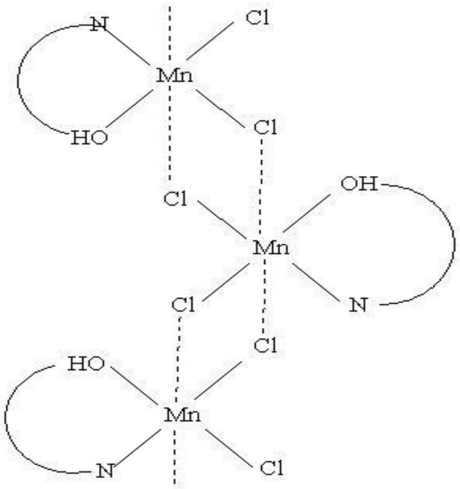

Figure 3a   Structure of $MnCl_2$.DEBQ

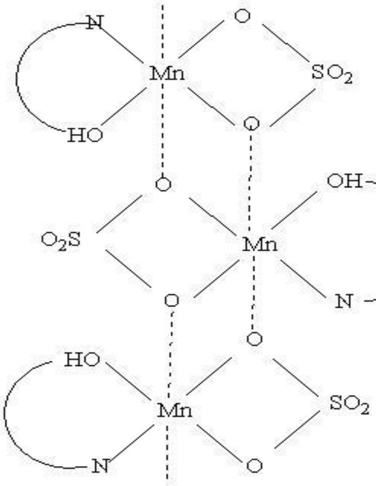

Figure 3c Structure of $MnSO_4$.DEBQ

Where=   N ⌒ OH is DEBQ

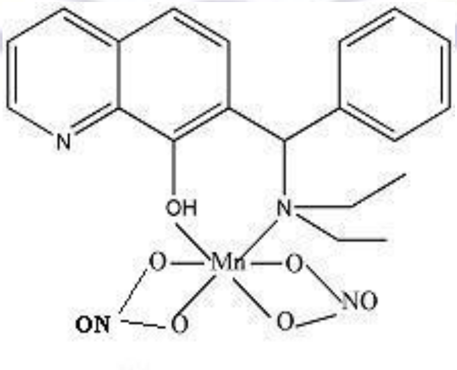

Figure 3b Structure of $Mn(NO_3)_2$.DEBQ

The blue coloured Ni^{II} chloro complex exhibits absorption bands at 4300,8670 ,15040 and 28720cm^{-1} .These bands are attributed to $^3T_1(F)\rightarrow{}^3T_2(F)$,$^3T_1(F)\rightarrow{}^3A_2(F)$ and $^3T_1(F)\rightarrow{}^3T_1(P)$ and charge transfer(CT) transitions respectively. The ν_2/ν_1 ratio for the chloro complex of Ni^{II} is observed at 2.016. This value is within the stipulated range 2.000-2.242 pointing to the tetrahedral stereochemistry for the Ni^{II} chloro complex.The Ni^{II} nitrato complex is also blue in colour and shows electronic absorption bands at 3860,8370,15100 and 28820cm^{-1} and these absorption are attributed to $^3T_1(F)\rightarrow{}^3T_2(F)$, $^3T_1(F)\rightarrow{}^3A_2(F)$, $^3T_1(F)\rightarrow{}^3T_1(P)$ and CT transitions respectively. The v_2/v_1, ratio for the nitrato nickel(II)complex is also with in stipulated range for the tetrahedral geometry. The Ni^{II} sulphato complex measures absorptions at 3990, 8720, 15207 and 28490cm^{-1} which are attributed to $^3T_1(F)\rightarrow{}^3T_1(F)$,$^3T_1(F)\rightarrow{}^3A_2$ (F),$^3T_1(F)\rightarrow{}^3T_1(P)$ and CT respectively. The v_2/ v_1 ratio for this complex is measured at 2.185 which is within the stipulated range for the tetrahedral geometry. Hence the Ni^{II} sulphato complex is assigned a tetrahedral geometry on the basis of the electronic spectrum.

Sl.No.	Complex	Colour (μ_{eff} B.M)	Absorption Maxima(cm^{-1})	Transition Assignments
1	$MnCl_2$.DEBQ	Brown (5.18)	13205 22510 25220	$^6A_{1g}\rightarrow{}^4T_{1g}$ $^6A_{1g}\rightarrow{}^4A_{1g}+{}^4E_g$ $^6A_{1g}\rightarrow{}^4T_{2g}$
2	$Mn(NO_3)$.DEBQ	Brown (5.25)	12670 22760 25160	$^6A_{1g}\rightarrow{}^4T_{1g}$ $^6A_{1g}\rightarrow{}^4A_{1g}+{}^4E_g$ $^6A_{1g}\rightarrow{}^4T_{2g}$
3	$MnSO_4$.DEBQ	Brown (5.30)	13150 22480 25380	$^6A_{1g}\rightarrow{}^4T_{1g}$ $^6A_{1g}\rightarrow{}^4A_{1g}+{}^4E_g$ $^6A_{1g}\rightarrow{}^4T_{2g}$
4	$NiCl_2$.DEBQ	Blue (4.14)	4300 8670 15070 28720	$^3T_1(F)\rightarrow{}^2T_2$ (F) $^3T_1(F)\rightarrow{}^2A_2$ (F) $^3T_1(F)\rightarrow{}^2T_1(P)$ CT
5	$Ni(NO_3)_2$.DEBQ	Blue (4.23)	3860 8370 15100 28833	$^3T_1(F)\rightarrow{}^2T_2$ (F) $^3T_1(F)\rightarrow{}^2A_2$ (F) $^3T_1(F)\rightarrow{}^2T_1(P)$ CT
6	$NiSO_4$.DEBQ	Blue (4.19)	3990 8720 15207 28490	$^3T_1(F)\rightarrow{}^2T_2$ (F) $^3T_1(F)\rightarrow{}^2A_2$ (F) $^3T_1(F)\rightarrow{}^2T_1(P)$ CT

Table-3 Colours, electronic spectral and magnetic data for Mn^{II} and Ni^{II} complexes of DEBQ

The μ_{eff} values of the chloro, nitrato and sulphato complexes of nickel are measured at 4.14, 4.23 and 4.19 B.M respectively. These values indicate a four coordinate tetrahedral geometry around the Ni^{II} in these complexes.(Figure 4)

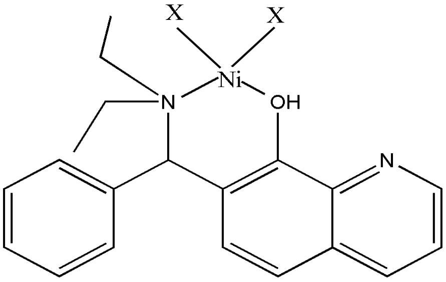

Figure 4 Structure of Ni^{II} complexes

where X=Cl,NO_3 ,0.5SO_4

Thermal decomposition studies

Thermal decomposition DEBQ

The ligand DEBQ is thermally stable upto 130^{0}C. It undergoes a two stage decomposition in the presence of air(Kamalakannan P and Venkappayya D, 2002).The first stage of decomposition is in the temperature range of 130-200^{0}C. This is shown by a broad DTG peak centered at 168^{0}C. The thermogram (Figure 5) shows the existence of an intermediate in the temperature range 200-300^{0}C, the composition of which is not clearly understood. The intermediate undergoes further decomposition (second stage) and complete weight loss at 300-430^{0}C. The decomposition of the intermediate is shown by another DTG peak centered at 363^{0}C. However the DTA plot is not very clear.

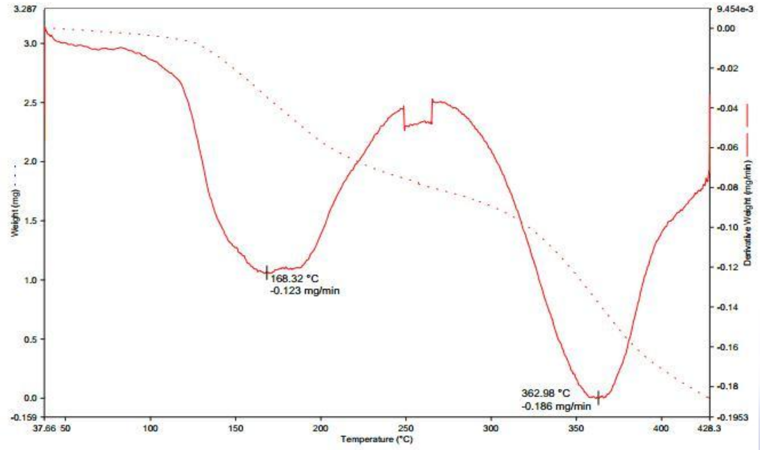

Figure 5 TG/DTG patterns of DEBQ

Thermal decomposition $MnCl_2$ .DEBQ

The thermal decomposition study on $MnCl_2$.DEBQ shows a two stage decomposition pattern (Figure 6). The sample experiences a small initial weight loss due to elimination of adsorbed water. The onset of decomposition of the dry complex begins at 163^{0}C. There is a rapid weight loss of 30% in the range 163-230^{0}C due to the elimination of the organic ligand (DEBQ) to form the metal chloride as the intermediate. This first stage of decomposition is indicated by the DTG peak found at 194-214^{0}C. The $MnCl_2$ intermediate formed undergoes gradual decomposition in the range 475-525^{0}C. It is indicated by the DTG peak centered at 505^{0}C. The oxide of manganese is the final residue produced.The DTA peak obtained is not useful to indicate the changes involved in the thermal decomposition.

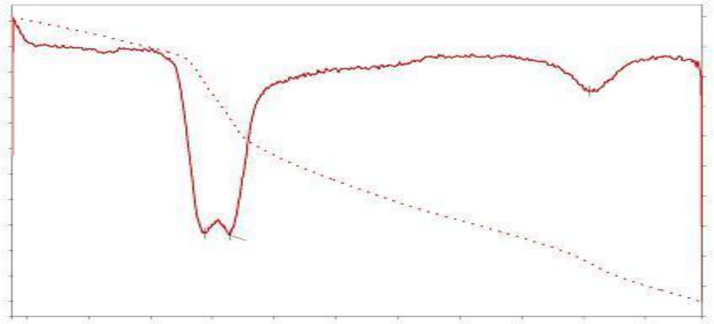

Figure 6 TG/DTG patterns of $MnCl_2$.DEBQ

Thermal decomposition $Ni(NO_3)_2$.DEBQ

$Ni(NO_3)_2$.DEBQ also displays a two stage thermal decomposition as shown in Figure 7. The compound experiences a small weight loss in the beginning of heating due to loss of adsorbed water. The dry complex is stable upto 180 ^{0}C and it decomposes in the temperature range 180-325^{0}C. This first stage of decomposition involves elimination of DEBQ and the formation of $Ni(NO_3)_2$. as the intermediate. This decomposition is evidenced by the DTG peak centered at 245^{0}C. The intermediate $Ni(NO_3)_2$ undergoes further decomposition(second stage) to produce NiO as the final residue. The decomposition of $Ni(NO_3)_2$ to produce NiO is supported by the DTG peak centering at 514^{0}C. The weight of the final residue is found to be at 16% of the original anhydrous complex. In this thermal decomposition study also the DTA pattern is not useful to follow the information given by TG.

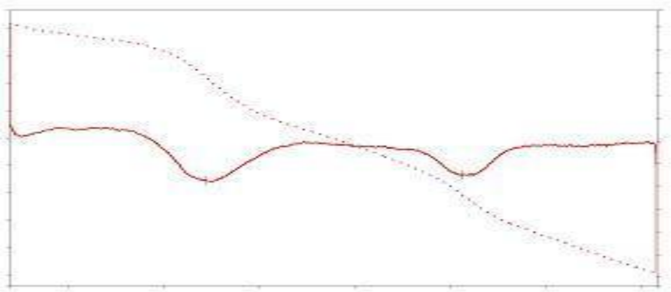

Figure 7 TG/DTG patterns of $Ni(NO_3)_2$.DEBQ

Antimicrobial studies

The Mannich base ligand (DEBQ) and its Mn^{II} and ***Ni^{II}*** chloro complexes have been screened for antimicrobial activity against *E.coli, S.aureus, A.niger* and *P.chrysogenum*. The levels of antimicrobial activity in terms of the zones of inhibition produced by the test compounds are presented in Table 4. The Mannich base is highly active against both the bacterial and the fungal strains tested. The Mannich base ligand exhibits comparable activity with the standard antibacterial drug used (ampicillin). But antifungal activity the Mannich base is more potent than that of standard drug (amphotericin – B). It shows that this organic compound may very well be used as an antifungal antibiotic. The mangese(II) complex exhibits more significant activity than the nickel(II) complex against both the bacterial and the fungal organisms tested.

Compound	**Zone of Inhibition (mm)**							
	E.coli		***S.aureus***		***A.niger***		***P.chrysogenum***	
	50 (µg/mL)	100 (µg/mL)	50 (µg/mL)	100 (µg/mL)	50 (µg/mL)	100 (µg/mL)	50 (µg/mL)	100 (µg/mL)
DEBQ	18	24	39	41	17	19	19	24
$MnCl_2$.DEBQ	16	10	27	32	16	20	20	23
$NiCl_2$.DEBQ	14	18	17	19	11	12	10	11
Ampicillin	-	27	-	28	-	-	-	-
Amphotericin-B	-	-	-	-	-	11	-	10

Table 4 Antimicrobial activity of DEBQ and its metal chloro complexes

Conclusion

Manganese(II) and nickel(II) ion complexes of 7-diethylaminobenzyl-8-hydroxyquinoline have been synthesized and their spectral, thermal and antimicrobial properties have been investigated. Though this ligand has several binding sites it prefers to coordinate to the metal ion through the phenolic oxygen and the diethylamino nitrogen atoms. The structures of the coordination compounds prepared have been established based on analytical and spectral data as shown in Figures

3a-c and 4. From antimicrobial screening studies it is concluded that the Mannich base ligand is possessing more significant activity than the metal complexes as well as the standard drugs employed . Among the coordination compounds investigated manganese(II) complex is more active than nickel(II).The complexes undergo two stage thermal decomposition to form metal oxides as final residues.

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