SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL SCREENING OF NOVEL TRANSITION METAL COMPLEXES OF MANNICH BASE 7-((DIPHENYLAMINO) (4-CHLOROPHENYL) METHYL) QUINOLIN-8-OL

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Abstract: A novel ligand mannich base 7-((diphenylamino) (4-chlorophenyl) methyl) quinolin-8-ol was synthesized by condensation method. The transition metal ion Co (II), Mn (II), Cu (II), Ni (II) and Zn (II) acetate salts were incorporated with Mannich base to form metal-ligand complexes. The novel synthesized ligand and their metal-ligand complexes have been elucidated by H^1 NMR, IR and mass spectral data. The prepared compound (Ligand) and metal ion complexes were screened against the Gram +Ve and Gram –Ve bacteria. Almost all complexes showed good antibacterial activity. In particular, Copper, Nickel and Zinc metal ion complexes showed best antibacterial activity.

Key-words: Mannich base 7-((diphenylamino) (4-chlorophenyl) methyl) quinolin-8-ol, Transition Metal-Ligand complexes, Antibacterial activity.

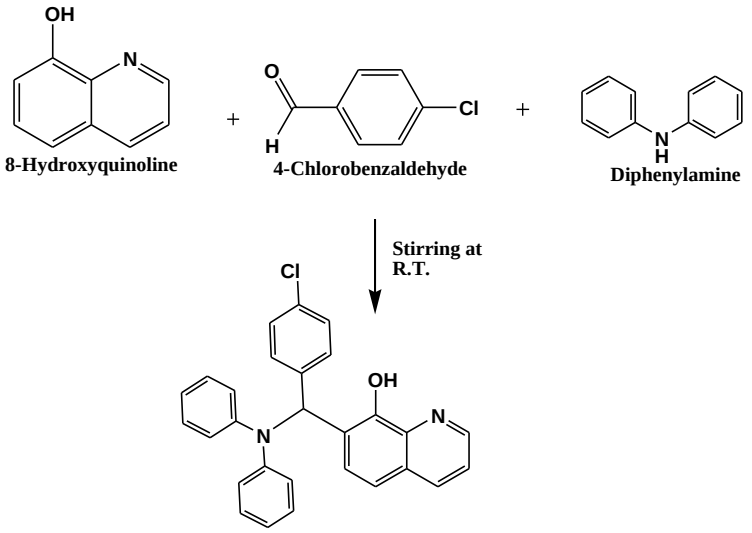
INTRODUCTION

8-Hydroxyquinoline (8HQ) (Figure 1), a quinoline derivative originating in plants as well as from synthesis, has been used as a fungicide in agriculture and a preservative in the textile, wood, and paper industries. [1] 8HQ possesses potent coordinating ability and good metal recognition properties, which means it is widely used for analytical and separation purposes as well as for metal chelation [2] Metal ions play a very important role in biological processes, and metal homeostasis is required for the maintenance of metal balance. [3, 4] Many diseases arise from the loss of homeostasis including metal overload and deficiency, which are caused by abnormal metal metabolism or metal absorption. Of all the hydroxyquinoline derivatives, 8HQ is the most interesting one to be explored, owing to its multifunctional properties, such as diverse bioactivities and therapeutic potentials [5-6].

MATERIALS AND METHODS

Synthesis of 7-((diphenylamino) (4-chlorophenyl) methyl) quinolin-8-ol (L) and its properties:

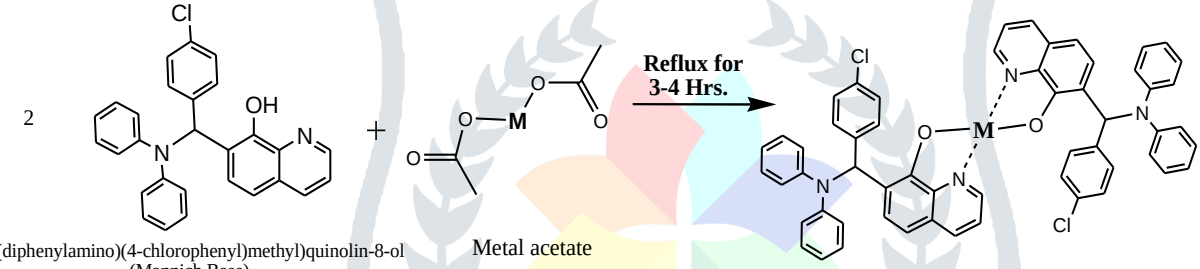
8-Hydroxyquinoline was condensed with 4-Chlorobenzaldehyde and diethylamine in 1:1:1 mole ratio at room temperature in acetone medium. Thus, an amount of 14.51g(0.1M) of 8-hydroxyquinoline in 25mL of acetone was continuously stirred with 14.00g (0.1M) of 4-Chlorobenzaldehyde and 7.3g (0.1M) of diethylamine using a magnetic stirrer. The clear solution became a semisolid after a few hours and a sandal yellow colored crude product was obtained after a few days. The crude product was crushed in to powder, washed repeatedly with cold water and recrystallized from methanol. The purity of the product was checked by TLC. The product was insoluble in water but freely soluble in several organic solvents such as ethanol, methanol, acetone, DMSO, DMF, benzene etc., and it was stable in air and nonhygroscopic. The formation of the new Mnnich base is illustrated in Scheme 1.



7-((diphenylamino)(4-chlorophenyl)methyl)quinolin-8-ol

Preparation of complexes:

Metal salt (0.01 M) and the mannich Base (0.02M) were dissolved in 20 ml of hot ethanol separately. These two solutions were slowly mixed at very hot condition and stirred vigorously and refluxed for 3 to 4 Hrs. Solid product with characteristic color was form within few minute and it was filter off and washes with ethanol and dried and the yield and color physical nature were noted.



M = Co^{++},Mn^{++},Cu^{++},Ni^{++},Zn^{++}

INSTRUMENTATION:

FT-IR spectra in the range, 4000-200 cm^{-1}, were recorded on 8300 Shimadzu Spectrophotometer, UV-visible spectra were measured by using Shimadzu 160 spectrophotometer in the range 200-1000 nm. The magnetic susceptibility values of the prepared complexes were obtained at room temperature using Magnetic Susceptibility on Bruker Magnet B.M.6, The ^1H nuclear magnetic resonance spectra were recorded on a BRUKER ADVANCED II 400 MHz spectrometer in DMSO as a solvent, relative to the internal standard Tetramethylsilane (TMS). Melting points were recorded on a Tanco Laboratory melting point apparatus.

Sr. No	Compound	Recrystallized by	Molecular formula	% yield	Color	Melting point
	Ligand	Ethanol	$C_{28}H_{21}ClN_2O$	63%	Blood red	145^0C
1	Co Complex	Ethanol	$C_{56}H_{40}C_{l2}CoN_4O_2$	65%	Pink	185^0C
2	Mn Complex	Ethanol	$C_{56}H_{40}C_{l2}N_4MnO_2$	74%	Grayish	192^0C
3	Cu Complex	Ethanol	$C_{56}H_{40}C_{l2}N_4CuO_2$	75%	Light Yellow	195^0C
4	Ni Complex	Ethanol	$C_{56}H_{40}C_{l2}N_4NiO_2$	54%	Blue	178^0C
5	Zn Complex	Ethanol	$C_{56}H_{40}Cl_2N_4ZnO_2$	57%	Blue	190^0C

7-((diphenylamino) (4-chlorophenyl) methyl) quinolin-8-ol (L):

Solid, mp 145°C, **UV (λmax) in ethanol:** 245 nm, **(IR) υmax (KBr/cm-1):** 3127.41 (Ar-C-H), 2985.91 (Ali-C-H), 1685.81 (Ar-C=C), 1645.17 (Ar-C=N), 1329.22 (C-C), 1230.34 (C-N). **^{1}H-NMR (δ-ppm):** 5.33 (s, 2H, N-C-H), 6.68 (d, Ar-H), 7.02 (d, Ar-H), 7.04 (dd, Ar-H), 7.15 (d, Ar-H), 7.22(d, Ar-H), 7.48 (d, Ar-H), 7.83(d, Ar-H), 8.87(dd, Ar-H), 10.85(s, Ar-O-H).

Bis-(7-((diphenylamino) (4-chlorophenyl) methyl) quinolin-8-ol Cobalt (II) Complex (ML1) :

Solid, mp 185°C, **UV (λmax) in ethanol:** 266 nm, **(IR) υmax (KBr/cm-1):** 724.82 **(**Co-O stretching), 3023.45 (Ar-C-H), 2945.51 (Ali-C-H), 1699.20 (Ar-C=C), 1642.41 (Ar-C=N), 1370.30 (C-C), 1225.41 (C-N), 1122.53 (C-O). **^{1}H-NMR (δ-ppm):** 3.45 (s, 2H, N-C-H), 6.84 (d, Ar-H), 7.20 (d, Ar-H), 7.08 (dd, Ar-H), 7.12 (d, Ar-H), 7.28(d, Ar-H), 7.30 (d, Ar-H), 7.80(d, Ar-H), 7.89 (dd, Ar-H).

Bis-(7-((diphenylamino) (4-chlorophenyl) methyl) quinolin-8-ol Manganese(II) Complex (ML2):

Solid, mp 192°C **UV (λmax) in ethanol:** 275 nm, **(IR) υmax (KBr/cm-1):** 698.59 **(**Mn-O stretching), 3033.50 (Ar-C-H), 2950.51 (Ali-C-H), 1669.10 (Ar-C=C), 1644.11 (Ar-C=N), 1350.30 (C-C), 1235.12 (C-N), 1125.50 (C-O). **^{1}H-NMR (δ-ppm):** 3.55 (s, 2H, N-C-H), 6.74 (d, Ar-H), 7.30 (d, Ar-H), 7.10 (dd, Ar-H), 7.22 (d, Ar-H), 7.30(d, Ar-H), 7.40 (d, Ar-H), 7.70(d, Ar-H), 7.90 (dd, Ar-H).

Bis-(7-((diphenylamino) (4-chlorophenyl) methyl) quinolin-8-ol Copper (II) Complex (ML3) :

Solid, mp 195°C **UV (λmax) in ethanol:** 286 nm, **(IR) υmax (KBr/cm-1): 860**.30 **(**Cu-O stretching), 3007.40 (Ar-C-H), 2936.11 (Ali-C-H), 1690.15 (Ar-C=C), 1618.23 (Ar-C=N), 1364.20 (C-C), 1221.15 (C-N), 1105.20 (C-O). **^{1}H-NMR (δ-ppm):** 3.76 (s, 2H, N-C-H), 6.73 (d, Ar-H), 7.40 (d, Ar-H), 7.20 (dd, Ar-H), 7.25 (d, Ar-H), 7.33(d, Ar-H), 7.42 (d, Ar-H), 7.77(d, Ar-H), 7.86 (dd, Ar-H).

Bis-(7-((diphenylamino) (4-chlorophenyl) methyl) quinolin-8-ol Nickel (II) Complex (ML4) :

Solid, mp 178°C **UV (λmax) in ethanol:** 263 nm, **(IR) υmax (KBr/cm-1):** 728.80 **(**Ni-O stretching), 3025.40 (Ar-C-H), 3000.11 (Ali-C-H), 1650.30 (Ar-C=C), 1646.20 (Ar-C=N), 1373.15 (C-C), 1230.45 (C-N), 1133.50 (C-O). **^{1}H-NMR (δ-ppm):** 3.35 (s, 2H, N-C-H), 6.74 (d, Ar-H), 7.30 (d, Ar-H), 7.10 (dd, Ar-H), 7.15 (d, Ar-H), 7.30(d, Ar-H), 7.32 (d, Ar-H), 7.69 (d, Ar-H), 7.77 (dd, Ar-H).

Bis-(7-((diphenylamino) (4-chlorophenyl) methyl) quinolin-8-ol Zinc (II) Complex (ML5) :

Solid, mp 190°C **UV (λmax) in ethanol:** 255 nm, **(IR) υmax (KBr/cm-1):** 730.82 **(**Zn-O stretching), 3055.55 (Ar-C-H), 3025.50 (Ali-C-H), 1669.10 (Ar-C=C), 1650.45 (Ar-C=N), 1375.20 (C-C), 1230.11 (C-N), 1133.51 (C-O). **^{1}H-NMR (δ-ppm):** 3.55 (s, 2H, N-C-H), 6.74 (d, Ar-H), 7.12 (d, Ar-H), 7.03 (dd, Ar-H), 7.10 (d, Ar-H), 7.30(d, Ar-H), 7.32 (d, Ar-H), 7.79(d, Ar-H), 7.81 (dd, Ar-H).

PHARMACOLOGY

Antibacterial activity

The title compounds were screened for their antibacterial activity using disc diffusion method. The bacterial organisms used included both gram positive and gram negative strains like Staphylococcus aureus, Escherichia coli, Streptococcus pyogens, Salmonella enteric Ser para typhi, S.entrica ser typhi and Micrococcus luteus.

For antibacterial susceptibility testing of title compounds, the sterile disc of 6 mm diameter (SD067, HiMedia, Mumbai) was loaded with 20µl of title compound solution (1000 µg/ml) in DMF. The discs were then placed at centre on the Mueller-Hinton agar seeded with bacterial inoculums approximately 106 CFU/ ml, incubated at 37° C for 24 hrs and growth inhibition zone formed around disc was measured. Test was done in triplicate and mean value was considered as inhibition zone. Solvents were used as controls and showed no inhibitions in preliminary studies. All the synthesized complexes exhibited moderate to good activity against the test organisms. [7]

Table 5: antimicrobial activity

Ligand (L), Co complex (ML1), Mn complex (ML2), Cu complex (ML3), Ni complex (ML4), Zn complex (ML5);
+++ = Zone size 16-22 mm; ++= Zone size 9-15 mm; + = Zone size 6-8 mm; — = No inhibition.

CONCLUSION

The ligand 7-((diphenylamino) (4-chlorophenyl) methyl) quinolin-8-ol (L) and its Mn (II), Co (II), Cu (II), Ni (II) and Zn (II) complexes have been synthesized by condensation methods. Their spectral properties were studied by UV, IR & H1NMR spectroscopic methods. The Mannich base ligand prefers to coordinate through the phenolic oxygen and aromatic nitrogen atoms based on analytical and spectral studies. Among the ligands and metal-ligand complexes Copper, Nickel and Zinc complexes showed best activity against the gram positive and gram negative bacteria where as other complexes and ligand shows moderate activity.

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Compound	Gram negative bacteria			Gram positive bacteria		
	S. enterica Ser typhi	Salmonella enterica Serpara typhi	E.Coli	Streptococcus pyrogens	Micrococcus luteus	S.aureus
L	-	-	++	++	-	-
ML 1	+	+	+	-	-	+
ML 2	-	+	-	++	+	++
ML 3	++	++	++	++	+	++
ML 4	++	+	+++	++	++	+
ML 5	++	+++	++	++	+	++