



SYNTHESIS, SPECTRAL AND ANTIMICROBIAL STUDIES OF SOME TRANSITION METAL(II) COMPLEXES WITH SCHIFF BASE 3-[(2-HYDROXY-6-METHOXYQUINOLIN-3-YLMETHYLENE)-AMINO]-2-METHYL-3H-QUINAZOLINE-4-ONE

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ABSTRACT : The Complexes of the type ML_2 and $M'L$ [where $M = Cu(II), Co(II), Ni(II)$ and $Mn(II)$; $M' = Zn(II), Cd(II)$ and $Hg(II)$] with the Schiff base ligand (HMeOQMAMQ) $L = 3-[(2-hydroxy-6-methoxyquinolin-3-ylmethylene)-amino]-2-methyl-3H-quinazoline-4-one$, have been synthesized. Their characterizations have been done by elemental analysis, conductance data, magnetic susceptibility measurements, 1H NMR, electronic, IR, ESR and X-ray studies. Ligand field parameters of some of the complexes have also been calculated. On the basis of spectral studies, the complexes of $Zn(II), Cd(II)$ and $Hg(II)$ have been assigned tetrahedral geometry, where as complexes of $Co(II), Ni(II)$ and $Mn(II)$ have been assigned octahedral geometry, The complex of $Cu(II)$ has been assigned distorted octahedral geometry. The Schiff base ligand and its complexes have also been screened for their antimicrobial activity against selected fungi and bacteria. The antimicrobial results indicate that the metal complexes act as better antimicrobial agents as compared to the Schiff base ligand.

Key Words: Complex; quinoline; quinazoline; antimicrobial activity

INTRODUCTION

Quinazolines and condensed quinazolines exhibit diverse pharmacological activities (Padia et al., 1998). Quinazolines are a big family of heterocyclic compounds, which have shown broad variety of antitumor activity (Xia et al., 2001, Yesilada et al., 2004). Amino quinazoline derivatives were found to be phosphodiesterase property (Segarra et al., 1998), and they work as potent anticancer agents (Hong et al., 2010). Among the various quinazolines reported, the substituted quinazolines exhibit interesting pharmacological activities like anticonvulsant (Al-Shaalan, 2007), antibacterial (Al-Shaalan, 2011) and anti-inflammatory (El-Behery et al., 2007), analgesic activities (Berndt et al., 2010). Some substituted quinazolines have been found to be potential and highly selective antiplasmodial activity (Verhaeghe et al., 2008, Verhaeghe et al., 2009). New quinazolines derivatives displaying anticancer precursors (Kabri et al., 2009, Kabri et al., 2010). Dimethylquinazolin-4-amine acts as a potent apoptosis inducer and efficacious anticancer agent with high blood brain barrier penetration (Sirisoma et al., 2009). They are also used to work out specific anti-hepatocellular carcinoma agents and colon cancer cell growth (Zeng et al., 2010). Quinazoline Schiff bases possess potent analgesic and anti-inflammatory activities (Kenichi et al., 1985). Among the other pharmacological activities, quinazoline derivatives show remarkable antimicrobial properties against microorganisms associated with death in patients due to immunocompromised diseases (Foote et al., 2008, Michael, 1999).

A literature survey reveals that, the reaction of methyl quinazoline hydrazide and methoxy quinoline aldehyde Schiff base ligand has not been reported so far. Hence, it was thought worthwhile to synthesize new substituted quinazoline ligand (HMeOQMAMQ) and its metal(II) complexes.

The present work discusses the synthesis, spectral and antimicrobial studies of the complexes of $Cu(II), Co(II), Ni(II), Mn(II), Zn(II), Cd(II)$ and $Hg(II)$ with the following ligand (HMeOQMAMQ) (figure 1).

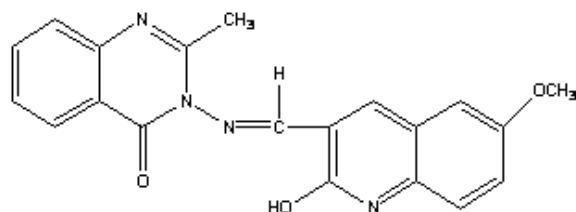


Figure-1: Structure of the ligand (HMeOQMAMQ)

Experimental

All the reagents used were of analytical grade and used without further purification. The metal chlorides / salts were of E. Merck and used as received.

Synthesis of 3-amino-2-methylquinazoline-4-one

A mixture of methyl-N-acetyl anthranilate (0.1 mol) and hydrazine hydrate (0.1 mol) in ethanolic solution was refluxed for 6 hours. The excess of solvent was then distilled off, and the resulting solid was dried and recrystallised from absolute ethanol (Alagarsamy et al., 2003, Sahu et al., 2008) (m.p. 186°C, yield 75%).

Preparation of 3-formyl-2-hydroxy-6-methoxyquinoline

A mixture of 2-chloro-3-formyl-6-methoxyquinoline (2.4 g, 0.01 mol) and aqueous hydrochloric acid (35 ml, 4 mol) was heated under reflux on water bath for about 1 hour and then allowed to cool to room temperature. 3-formyl-2-hydroxy-6-methoxyquinoline separated as solid, was collected by filtration and recrystallized from aqueous acetic acid into yellow silky needles (m.p. 185 °C, yield 65%).

Synthesis of ligand: Preparation of 3-[(2-hydroxy-6-methoxyquinolin-3-yl)methylene]-amino]-2-methyl-3H-quinazoline-4-one (HMeOQMAMQ)

The ligand (HMeOQMAMQ) was prepared by the reaction of 3-amino-2-methyl quinazoline-4-one (0.01 mol) with 3-formyl-2-hydroxy-6-methoxyquinoline (0.01 mol) in ethanol by refluxing on water bath for 6-7 hours in the presence of a few drops of acetic acid. The reaction mixture was cooled to room temperature, the separated ligand was filtered, washed and recrystallized from alcohol. The purity of the ligand (HMeOQMAMQ) was checked by TLC (m.p. 251°C, yield 70%) (Figure 2).

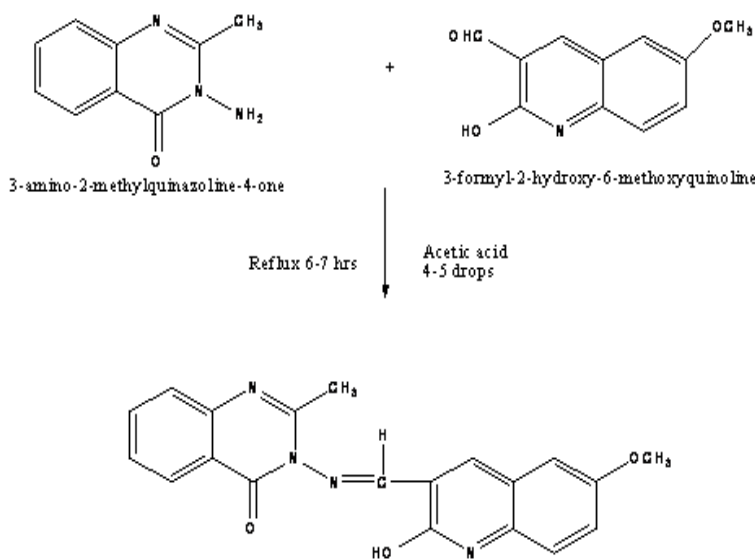


Figure-2: Scheme for preparation of ligand (HMeOQMAMQ)

Preparation of complexes

To the hot solution of the Schiff base ligand (HMeOQMAMQ) (0.001 mol) in ethanol (35 ml), a hot ethanolic solution of respective metal chlorides (0.001 mol) in ethanol (15 ml) was added and the reaction mixture was then treated with sodium acetate (0.5 g) and the refluxing was continued further for 2 hours. The resulting reaction mixture was then decomposed by pouring into distilled water (90-100 ml), the colored complex separated out was collected by filtration, washed with distilled water, then with hot ethanol and dried in vacuum over anhydrous calcium chloride. The complexes were analyzed for their metal and chloride contents by standard methods (Vogel., 1962). Elemental analysis data is shown in Table 1.

Physical Measurements

The molar conductance of the complexes was measured on ELICO CM-82 Conductivity Bridge in DMF solution at a concentration of 10^{-3} M. Magnetic susceptibilities were measured on a Guoy balance at room temperature using Hg[Co(SCN)₄] as calibrant. Infrared spectra of the ligand and its metal (II) complexes in KBr pellets were recorded in the spectral range 4000 - 350 cm^{-1} with Perkin Elmer Spectrum one FT-IR spectrometer. UV-Visible spectra were recorded on an Elico SL-164 DOUBLE BEAM UV-Vis Spectrophotometer in the range of 200-1200 nm. ¹H NMR spectra were recorded on AMX-400 NMR spectrometer, using TMS as internal standard and DMSO as a solvent. X-ray diffraction spectrum was obtained on the Philips P.W.3710 diffractometer at CIL, University of Hyderabad, Hyderabad. The elemental analysis (CHN) were obtained from Thermo finnigam, Italy, FLASH EA 1112 series and ESR spectra recorded on VARIAN, USA, E-112 Spectrometer at IIT Bombay.

RESULTS AND DISCUSSION

The analytical data indicates that the stoichiometry of the complexes are 1:2 (metal to ligand ratio) for Cu(II), Co(II), Ni(II) and Mn(II) and 1:1 (metal to ligand ratio) for Zn(II), Cd(II) and Hg(II) complexes. The prepared complexes were sparingly soluble in common organic solvents but soluble in DMF, DMSO and acetonitrile. The observed molar conductance values measured in DMF solution fall in the range 14-20 $\text{Ohm}^{-1} \text{cm}^2 \text{mol}^{-1}$, indicating that the complexes are non-electrolytic in nature (Geary 1971).

Magnetic susceptibility measurements

The present Cu(II) complex has a magnetic moment value 1.97 B.M. The magnetic moment value observed for Cu(II) complex under present study is due to distorted octahedral geometry (Lever 1984, Vashi et al., 2010). The mononuclear Cu(II) complex having no major spin interaction shows magnetic moment in the range of 1.75-2.20 B.M. The spin free octahedral complex of Co (II) are reported to exhibit magnetic moment in the range of 4.70-5.53 B.M. (Abdalrazaq, et al., 2010). The Co (II) complex shows magnetic moment of 4.84 B.M. The magnetic moment value obtained for the Co (II) complex under study indicates that it has an octahedral configuration. For Ni (II) complex, the observed magnetic moment value is 3.24 B.M., which is well within the expected range for Ni (II) complex with octahedral geometry 2.83-4.0 B.M. (Agarwal, et al., 2006). The magnetic moment value of Mn (II) complex is 5.74 B.M., indicating it to be high spin type paramagnetic, which lies within the octahedral range, which is very close to spin only value of 5.90 B.M. as the ground term is ³A_{2g} and thus supports the octahedral stereochemistry (Vashi, et al., 2010). The Zn (II), Cd (II) and Hg(II) complexes showed a diamagnetic behavior. The magnetic susceptibility measurements of the complexes were performed at room temperature (Table 1).

Electronic spectra

The electronic spectral data of Cu(II), Co(II), Ni(II) and Mn(II) complexes of the ligand (HMeOQMAMQ) were recorded in DMF solution at 10^{-3} M concentration and are given in Table 2. The Cu(II) complex exhibits a broad asymmetric band in the region 12275-16350 cm^{-1} with a maxima at 1425 cm^{-1} in an distorted octahedral geometry (Reddy et al., 1987). The broadness of the band may be due to dynamic Jahn-Teller distortion and is assigned to ²T_{2g} → ²E_g transitions.

The electronic spectra of the Co(II) complex gave two absorption bands at 10150 cm^{-1} and 20150 cm^{-1} , due to ⁴T_{1g}(F) → ⁴A_{2g}(F)(v₁) and ⁴T_{1g}(F) → ⁴T_{1g}(P)(v₃) transitions. The bands due to the ⁴T_{1g}(F) → ⁴A_{2g}(F)(v₂) transitions could not be observed because of its very low intensity.

Table 1: Physical and analytical data of the ligand and its metal (II) complexes

| Ligand / Complex | Mol. Wt. | M.P. (°C) | Yield (%) | Found / (Calculated) % | | | | | μ_{eff} B.M. | Molar Conductance $\lambda_M \text{ Ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$ |
|--|----------|-----------|-----------|------------------------|----------------|-------------------|------------------|----------------|-------------------------|--|
| | | | | C | H | N | M | Cl | | |
| $\text{C}_{20}\text{H}_{16}\text{N}_4\text{O}_3$ | 360.37 | 251 | 70 | 66.66 (69.71) | 4.48 (4.62) | 15.55 (16.20) | - | - | - | - |
| $[\text{Cu}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | 782.26 | 275 | 65 | 61.43 (61.83) | 3.87 (4.09) | 14.32 (14.85) | 8.12 (8.77) | - | 1.97 | 16.25 |
| $[\text{Co}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | 777.65 | 280 | 63 | 61.78 (62.43) | 3.89 (4.08) | 14.41 (14.83) | 7.58 (7.85) | - | 4.84 | 19.10 |
| $[\text{Ni}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | 777.41 | 284 | 66 | 61.80 (62.25) | 3.89 (4.10) | 14.41 (15.15) | 7.55 (7.95) | - | 3.24 | 19.55 |
| $[\text{Mn}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | 773.65 | 282 | 65 | 62.10 (64.78) | 3.91 (4.08) | 14.48 (15.110) | 7.10 (7.41) | - | 5.74 | 19.90 |
| $[\text{Zn}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)\text{Cl}]$ | 460.02 | 283 | 64 | 52.20 (54.08) | 3.29 (3.40) | 12.17 (12.61) | 14.21 (14.72) | 7.70 (7.98) | Diamag | 14.30 |
| $[\text{Cd}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)\text{Cl}]$ | 507.22 | 285 | 60 | 47.36 (48.50) | 2.98 (3.24) | 11.05 (11.67) | 22.16 (22.90) | 6.99 (7.55) | Diamag | 16.20 |
| $[\text{Hg}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)\text{Cl}]$ | 595.40 | 289 | 62 | 40.34 (41.34) | 2.54 (2.89) | 9.41 (9.97) | 33.69 (34.57) | 5.95 (6.36) | Diamag | 15.75 |

The position of ν_2 band has been calculated (15416 cm^{-1}) by using the equation $\nu_2 = \nu_1 + 10Dq$. These transitions suggest octahedral geometry for Co (II) complex (Venkatesha et al., 2011). The ligand field parameters such as Dq , B' , β and $\beta\%$ have been calculated by using band-fitting equation given by Billing and Underhill. The crystal field splitting energy (Dq) value of 821 cm^{-1} , is well within the range reported for most of the octahedral Co (II) complexes. The Co (II) complex under present investigation possess Racha parameter $B' 930 \text{ cm}^{-1}$. The Racha parameter B' is less than free ion value 971 cm^{-1} , suggesting a considerable orbital overlap and delocalization of electrons on the metal ion. The nephelauxetic ratio (β) for the present Co (II) complex is 0.95 cm^{-1} . This is less than one, suggesting partial covalency in the metal ligand bond. The values Dq , $\beta\%$, LFSE and ν_2/ν_1 suggest the octahedral geometry for Co (II) complex. The electronic spectrum of Ni(II) complex shows three bands at 10775 , 15225 and 25350 cm^{-1} (Table 2), assignable to ${}^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)(\nu_1)$, ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)(\nu_2)$ and ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)(\nu_3)$ transitions respectively. The values ν_2/ν_1 and $\beta\%$ further support the octahedral geometry around the Ni (II) ion (Rekha et al., 2010). The observed bands for Mn (II) complex are at 10275 , 15250 and 23450 cm^{-1} due to the transitions ${}^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)(\nu_1)$, ${}^3A_{2g}(F) \rightarrow {}^3A_{1g}(F)(\nu_2)$ and ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)(\nu_3)$ respectively. The position of bands indicates that the complex has six coordinated octahedral geometry (Sexana et al., 2010).

Table 2: Electronic spectral data and ligand field parameters of Cu (II), Co (II), Ni (II) and Mn (II) complexes (cm^{-1})

| Complexes | ν_1 | ν_2 | ν_3 | Dq | B' | β | $\beta\%$ | ν_2/ν_1 | ν_3/ν_2 | LFSE kcalmol^{-1} |
|---|---------|-------------|---------|------|------|---------|-----------|---------------|---------------|----------------------------|
| $[\text{Cu}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | - | 12275-16350 | | 1425 | - | - | - | - | - | 24.15 |
| $[\text{Co}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | 10150 | 15416 | 20150 | 821 | 930 | 0.95 | 15.28 | 1.51 | 1.30 | 14.16 |
| $[\text{Ni}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | 10775 | 15225 | 25350 | 934 | 836 | 0.82 | 19.87 | 1.41 | 1.66 | 31.85 |
| $[\text{Mn}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | 10275 | 15250 | 23450 | 937 | 864 | 0.79 | 22.56 | 1.48 | 1.53 | 16.50 |

Infrared spectra

The IR spectral data of the ligand (HMeOQMAMQ) and its metal (II) complexes are represented in Table 3. The broad band observed at 3375 cm^{-1} in the ligand (HMeOQMAMQ) is assigned to $\nu(\text{OH})$, which disappeared in all the complexes, thereby indicating the involvement of phenolic oxygen in bonding with metal ions through deprotonation (Milan et al., 2006). The sharp band observed at 1715 cm^{-1} in ligand is assigned to quinazoline ring $\nu(\text{C}=\text{O})$, which was shifted to $35\text{-}45\text{ cm}^{-1}$ in all complexes, indicating the involvement of carboxyl group of quinazoline ring ($\text{C}=\text{O}$) in complexation with metal ion (Sunil et al., 2011). The band exhibited at 1620 cm^{-1} is assigned to the azomethine $\nu(\text{C}=\text{N})$ group in the ligand, but in complexes it has lowered to $50\text{-}55\text{ cm}^{-1}$ due to the reduction of double bond character in carbon-nitrogen of the azomethine group (Giri et al., 2009).

The frequency observed at 1270 cm^{-1} of the ligand is attributed to phenolic $\nu(\text{C}-\text{O})$, but this band is shifted to higher frequency in the region $37\text{-}45\text{ cm}^{-1}$ for the complexes (Haseena et al., 2012). This confirms the involvement of phenolic OH in the complex formation. The low frequency skeletal vibrations due to $\text{M}-\text{O}$ and $\text{M}-\text{N}$ stretching provide direct evidence for complexation. In the present investigation the frequencies observed in the region of $520\text{-}540\text{ cm}^{-1}$ are due to $\nu(\text{M}-\text{O})$, and the frequencies observed in the region of $447\text{-}455\text{ cm}^{-1}$ are due to $\nu(\text{M}-\text{N})$ vibrations (El-tabl et al., 2010, Abdalrazaq et al., 2010). The frequencies observed in the region $350\text{-}355\text{ cm}^{-1}$ were due to $\nu(\text{M}-\text{Cl})$ bonding (Singh et al., 2010). These are characteristic of chlorine atom in $\text{Zn}(\text{II})$, $\text{Cd}(\text{II})$ and $\text{Hg}(\text{II})$ complexes and is further confirmed by quantitative chloride estimation.

^1H NMR spectra

The ligand (HMeOQMAMQ) showed sharp peak at $\delta 12.8$ (s, 1H) due to OH at 2-position of phenyl ring of quinoline moiety has resonated, but in the case of $\text{Zn}(\text{II})$ complex which disappeared indicate the involvement of phenolic oxygen in the coordination via deprotonation (Abou-Melha et al., 2008). The peak appeared at $\delta 8.8$ (s, 1H, $-\text{CH}=\text{N}$) is due to the azomethine group in the ligand, but in the case of $\text{Zn}(\text{II})$ complex the peak was observed at $\delta 8.5$ (s, 1H, $-\text{CH}=\text{N}$). The Schiff base ligand showed two separate singlet peaks at $\delta 2.80$ and $\delta 2.82$ (s, 2x3H) due to protons of the two $-\text{CH}_3$ groups which are attached to the quinazoline and quinoline moiety, but in $\text{Zn}(\text{II})$ complex it appears at $\delta 2.75$ and $\delta 2.77$. The one OCH_3 group of quinoline ring appeared at $\delta 3.48$ (s, 3H, OCH_3), which is shifted at $\delta 3.50$ in $\text{Zn}(\text{II})$ complex. The eight aromatic protons due to quinazoline and phenyl rings resonated in the region $\delta 7.00\text{-}8.70$ (m, 8H, Ar-H) as a multiplet, in $\text{Zn}(\text{II})$ complex the eight aromatic protons have been observed in the region $\delta 6.80\text{-}8.25$ (m, 8H, Ar-H) as a multiplet. On comparing the ^1H NMR spectra of the ligand (HMeOQMAMQ) and the $\text{Zn}(\text{II})$ complex, it was observed that the signals of protons of different functionalities of the ligand have been shifted to the downfield region indicating the coordination of the ligand to the metal $\text{Zn}(\text{II})$ ion.

Table 3: IR spectral data of the ligand and its metal (II) complexes (cm^{-1})

| Ligand/ complexes | ν_{OH} | $\nu_{\text{C}=\text{O}}$ | $\nu_{\text{C}=\text{N}}$ | $\nu_{\text{C}-\text{O}}$ | $\nu_{\text{M}-\text{O}}$ | $\nu_{\text{M}-\text{N}}$ | $\nu_{\text{M}-\text{Cl}}$ |
|--|-------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|----------------------------|
| $\text{C}_{20}\text{H}_{16}\text{N}_4\text{O}_3$ | 3375 | 1715 | 1620 | 1270 | - | - | - |
| $[\text{Cu}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | - | 1670 | 1570 | 1315 | 540 | 455 | - |
| $[\text{Co}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | - | 1675 | 1565 | 1310 | 535 | 451 | - |
| $[\text{Ni}((\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2)]$ | - | 1672 | 1568 | 1312 | 520 | 452 | - |
| $[\text{Mn}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)_2]$ | - | 1674 | 1567 | 1307 | 533 | 449 | - |
| $[\text{Zn}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)\text{Cl}]$ | - | 1676 | 1566 | 1312 | 535 | 447 | 355 |
| $[\text{Cd}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)\text{Cl}]$ | - | 1673 | 1567 | 1310 | 536 | 450 | 353 |
| $[\text{Hg}(\text{C}_{20}\text{H}_{15}\text{N}_4\text{O}_3)\text{Cl}]$ | - | 1671 | 1565 | 1313 | 537 | 452 | 350 |

ESR spectrum

The ESR spectrum of the Cu (II) complex was recorded at room temperature, on X-band at a frequency of 9.1 GHz under the magnetic-field strength of 3200G. One unpaired electron in Cu(II) complex with ${}^2B_{1g}$ as ground state lies in $d_{x^2-y^2}$ orbital and follows the trend $g_{\parallel} > g_{\perp} > g_{av}$. The analysis of spectra gives the data $g_{\parallel} = 2.290$, $g_{\perp} = 2.070$, $g_{av} = 2.042$, $g_{iso} = 2.195$ and $G = 4.845$ and are given in Table 4. The observed g_{\parallel} value for the Cu(II) complex was less than 2.3 which is in agreement with the covalent character of the metal ligand bond (Nagashria et al., 2011). The $G = (g_{\parallel} - 2)/(g_{\perp} - 2)$, which measures the negligible exchange interaction between the metal centers in polycrystalline solid, has been calculated. According to (Hathaway 1970) if $G > 4$, the exchange interaction is negligible, but if $G < 4$ it indicates considerable exchange interaction in the solid complex. The Cu(II) complex has the G value > 4 , indicating that the exchange interaction is negligible in solid complex. The observed value of $G = 4.845$ for the complex under the present study gives evidences of mononuclear nature of the complex.

Table 4: ESR data of the Cu (II) complex

| Complex | g_{\parallel} | g_{\perp} | g_{av} | g_{iso} | G |
|--|-----------------|-------------|----------|-----------|-------|
| [Cu(C ₂₀ H ₁₅ N ₄ O ₃) ₂] | 2.290 | 2.070 | 2.042 | 2.195 | 4.845 |

X-ray diffraction studies Cd(II) complex

The XRD data of Cd(II) complex are given in the Table 5. The Cd(II) complex has been characterized by powder XRD studies with a view to finding the type of crystal system. There are 3 reflections (2θ) between 6.5540° and 59.4240° with maxima at $2\theta = 59.4240^\circ$ corresponding to the value of $d = 1.804\text{\AA}$. The interplanar spacing (d) has been calculated from the positions of intense peaks using Braggs relation $n\lambda = 2d \sin\theta$ (where $\lambda =$ wavelength of X-ray used, $CuK\alpha = 1.5406\text{\AA}$). The observed and calculated values of d are quite consistent. The unit cell calculation has been carried out for the cubic system (Woolfson 1980).

The cell parameters have been calculated by using the equation for cubic system, $\sin^2\theta = \lambda^2/4a^2 (h^2+k^2+l^2)$, where $\lambda^2/4a^2$ is a common factor. The Cd(II) complex has a value of $\lambda^2/4a^2 = 0.0030$. The $h^2+k^2+l^2$ values are given in the Table 5. The absence of forbidden number indicates that the Cd(II) complex may belong to cubic symmetry. The complex showed broad peak indicating its amorphous nature.

Table 5: Powder X-ray diffraction data of Cd (II) complex

| Peak No. | 2θ | θ | $\sin\theta$ | $\sin^2\theta$ | $h^2+k^2+l^2$ | h k l | d | | | a in Å |
|----------|-----------|----------|--------------|----------------|---------------|--------|--------|--------|-----------|--------|
| | | | | | | | Calc. | Obs. | Intensity | |
| 1 | 6.554 | 3.277 | 0.057 | 0.003 | 1 | 1 0 0 | 17.210 | 17.211 | 14.65 | 17.211 |
| 2 | 32.330 | 16.165 | 0.278 | 0.077 | 33 | 5 2 2 | 3.142 | 3.142 | 42.10 | 17.211 |
| 3 | 59.424 | 29.712 | 0.495 | 0.245 | 105 | 10 2 1 | 1.804 | 1.804 | 100.00 | 17.211 |

Antimicrobial activity

The prepared ligand (HMeOQMAMQ) and its Cu(II), Co(II), Ni(II), Mn(II), Zn(II), Cd(II) and Hg(II) complexes have been tested for antimicrobial activity by cup-plate method (Barry 1991). The antimicrobial activity results of the screened compounds are given in the Table-6. Antibacterial activity against *E. coli* and *S. aureus* and antifungal activity against *A. niger* and *A. flavous* at $1000\mu\text{g/ml}$ concentration (Bauer, et al., 1966) were carried out. The standard drugs streptomycin and clotrimazole were also tested for their antibacterial and antifungal activity at the same concentration under the conditions similar to that of the test compounds (Jorgensen, et al., 2003).

The antibacterial activity results revealed that the ligand (HMeOQMAMQ) and its complexes show weak to good activity. The ligand and its Ni(II), Zn(II) Cd(II) and Hg(II) complexes are weakly active with the zone of inhibition 10-14 mm against both the organisms when compared with the standard drug streptomycin. The Mn(II) complex show moderate activity as compared with its ligand with the zone of inhibition 15-16 mm. The Cu(II) and Co(II) complexes exhibited good activity with the zone of inhibition 17-19 mm when compared with the standard drug streptomycin.

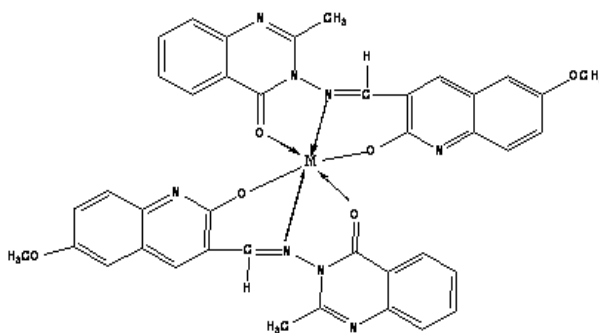
The antifungal activity results revealed that the ligand (HMeOQMAMQ) and its Cu(II), Co(II), Ni(II), Mn(II), Zn(II), Cd(II) and Hg(II) complexes exhibit weak to good activity. The ligand and its Ni(II), Cd(II) and Hg(II) complexes show weak activity 10-14 mm, when compared with the standard drug clotrimazole. The Zn(II) and Mn(II) complexes showed moderate activity as compared with its ligand with the zone of inhibition 15-16 mm. The Cu(II) and Co(II) complexes exhibited good activity with the zone of inhibition 17-19 mm when compared with the standard drug clotrimazole

Table 6: Antimicrobial activity of the ligand and its metal (II) complexes

| Compound | Antibacterial Activity zone of inhibition (in mm) | | Antifungal Activity zone of inhibition (in mm) | |
|--|--|------------------|---|-------------------|
| | <i>E. coli</i> | <i>S. aureus</i> | <i>A. niger</i> | <i>A. flavous</i> |
| C ₂₀ H ₁₆ N ₄ O ₂ | 11 | 10 | 10 | 11 |
| [Cu(C ₂₀ H ₁₅ N ₄ O ₂) ₂] | 19 | 17 | 18 | 19 |
| [Co(C ₂₀ H ₁₅ N ₄ O ₂) ₂] | 18 | 17 | 17 | 19 |
| [Ni((C ₂₀ H ₁₅ N ₄ O ₂) ₂)] | 12 | 13 | 13 | 14 |
| [Mn(C ₂₀ H ₁₅ N ₄ O ₂) ₂] | 16 | 15 | 15 | 15 |
| [Zn(C ₂₀ H ₁₅ N ₄ O ₂)Cl] | 13 | 14 | 15 | 16 |
| [Cd(C ₂₀ H ₁₅ N ₄ O ₂)Cl] | 12 | 13 | 13 | 13 |
| [Hg(C ₂₀ H ₁₅ N ₄ O ₂)Cl] | 12 | 13 | 12 | 13 |
| Streptomycin | 23 | 24 | - | - |
| Clotrimazole | - | - | 25 | 24 |
| DMF (Control) | 0 | 0 | 0 | 0 |
| Bore size | 08 | 08 | 08 | 08 |

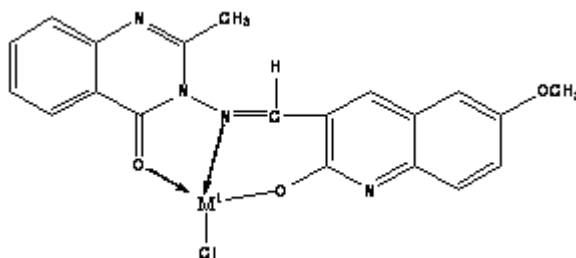
CONCLUSIONS

The elemental analysis, conductivity data, magnetic susceptibility, electronic, IR, ESR, ¹H NMR and X-ray diffraction spectral observations reveal the mononuclear nature of all the complexes. The non-electrolytic behavior of the complexes confirms the presence of chlorides within the coordination sphere. The Cu(II), Co(II), Ni(II) and Mn(II) complexes exhibit octahedral geometry, whereas Zn(II), Cd(II) and Hg(II) complexes exhibit tetrahedral geometry (Figure 3 and Figure 4). The prepared complexes show better antibacterial and antifungal activity than the ligand (HMeOQMAMQ)



Where M = Cu(II), Co(II), Ni(II) and Mn(II)

Figure-3: Structure of Cu(II), Co(II), Ni(II) and Mn(II) complexes



Where $M' = \text{Zn(II)}, \text{Cd(II)} \text{ and } \text{Hg(II)}$

Figure-4: Structure of Zn(II), Cd(II) and Hg(II) complexes

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REFERENCES

- A. Berndt, S. Miller, O. Williams, D.D. Le, B.T. Houseman, J.I. Pacold, F. Gorrec, W.C. Hon, P.D. Ren, Y. Liu, C. Rommel, P. Gaillard, T. Ruckle, M.K. Schwarz, K.M. Shokat, J.P. Shaw and R.L. Williams (2010), The p110 delta structure: mechanisms for selectivity and potency of new PI (3) K inhibitors. *Nat. Chem. Biol.*, 6, 117-124.
- A.B.P. Lever (1984), *Inorganic Electronic Spectroscopy*, 2nd Ed.; Elsevier: Amsterdam, The Netherlands.
- A.I. Vogel (1962), 'A Text Book of Quantitative Inorganic Analysis' 3rd Edn, ELBS and Longman Group Ltd. London.
- A.L. Barry (1991), 'Procedure and Theoretical consideration for testing antimicrobial agents in Agar media' 5th Edn, Williams wilkins Baltimore.
- A.S. El-tabl, F.A. Aly, M.M.E. Shakdofa and A.M.E. Shakdofa (2010), Synthesis, characterization and biological activity of metal complexes of azo hydrazone ligand, *J. Coord. Chem.* 63(4), 700-712.
- A.W. Bauer, W.M.M. Kirby, J.C. Sherris and M. Turck (1996), Antibiotic susceptibility testing by a standardized single disk method. *American J. Chem. Path.* 45, 493-496.
- A. Yesilada, S. Koyunoglu, N. Saygili, E. Kupeli, E. Yesilada, E. Bedir and I. Khan (2004), Synthesis, Antiinflammatory and Analgesic Activity Screening of some New 4(3-H)-Quina zolinone Derivatives. *Arch. Pharm. Pharm. Med. Chem.*, 337, 96-104.
- B.H. Banu, K. Bharathi and K.V.S.R.G. Prasad (2012), Synthesis, characterization and evaluation of *in vitro* antioxidant and anti-inflammatory activity of 2-(4-oxo-2-phenylquinazolin-3(4H)-yl) substituted acetic acids, *IOSR Journal of Pharmacy*, 2(1). 097-104.
- B.J. Hathaway and D.E. Billing (1970), *Coord. Chem. Rev.* 6, 143-180.
- E.A. Abdalrazaq, O.M.A. Ramadane and K.S. Al-Numa (2010), Synthesis and Characterization of Dinuclear Metal Complexes Stabilized by Tetradentate Schiff Base Ligands. *American J. Appl. Sci.* 7(5), 628-633.
- J.H. Jorgensen and J.D. Turnidge (2003), Susceptibility test methods: dilution and disk diffusion methods. *Manual of Clinical Microbiology*, 8th edn (Murray PR, Baron EJ, Jorgensen JH, Pfaller MA & Tenover FC, eds). American Society for Microbiology, Washington, DC. 1108.1127.
- J.K. Padia, M. Field, J. Hinton, K. Meecham, J. Pablo, R. Pinnock, B.D. Roth, L. Singh, N. Suman- Chauhan, B.K. Trivedi, and L. Webdale (1998), Novel Nonpeptide CCK-B Antagonists: Design and Development of Quinazolinone Derivatives as Potent, Selective, and Orally Active CCKB Antagonists. *J. Med. Chem.*, 41, 1042-1049.

- J.P. Michael (1999), Quinoline, quinazoline and acridone alkaloids. *Nat. Prod. Rep.* 16, 697- 709.
- K.M. Foote, A.A. Mortlock, N.M. Heron, F.H. Jung, G.B. Hill, G. Pasquet, M.C. Brady, S. Green, S.P. Heaton, S. Kearney, N.J. Keen, R. Odedra, S.R. Wedgea, and R.W. Wilkinson (2008), Synthesis and SAR of 1-acetanilide-4-aminopyrazole-substitutedquinazolines: Selective inhibitors of Aurora B kinase with potent anti-tumor activity. *Bioorg. Med. Chem. Lett.* 18, 1904-1909.
- K. Nagashria, J. Josepha and C. J. Dhanaraj (2011), Copper(II) complexes of hydroxyflavone derivatives as potential bioactive molecule to combat antioxidants: synthesis, characterization and pharmacological activities, *Appl. Organometal. Chem.* 25, 704–717.
- K.S. Abou-Melha and H. Faruk (2008), Bimetallic Complexes of Schiff Base Bis-[4-hydroxycoumarin-3-yl]thiocarbohydrazone as a Potentially Dibasic Pentadentate Ligand. *Synthesis, Spectral, and Antimicrobial Properties. J. Iran. Chem. Soc.* 5(1),122-134.
- K. Venkatesha, L.Venkata Reddy, K.B. Chandra Sekhar and K. Mukkanti (2011), Synthesis, Characterization and Antimicrobial Activity of Transition Metal Complexes of Schiff base, *International J. Chem.Tech. Research*, 3(2), 676-679.
- L.A. Abdalrazaq, O.M. Al-Ramadane and K.S. Al-Numa (2010), Synthesis and Characterization of Dinuclear Metal Complexes Stabilized by Tetradentate Schiff Base Ligands, *American J. Appl. Sci.* 7 (5): 628-633.
- L. Hong-Ze, H. Hai-Yun, H. Yuan-Yuan, L. H. Xin, Q. Qing-Rong, Z. Ying-Lan and L. Yang (2010), A General Synthetic Procedure for 2-chloromethyl-4(3*H*)-quinazolinone Derivatives and Their Utilization in the Preparation of Novel Anticancer Agents with 4-Anilinoquinazoline Scaffolds. *Molecules*, 15, 9473-9485.
- M. Cacic, M. Trkovic, F. Cacic and E. Has-Schon (2006), Synthesis and Antimicrobial Activity of Some Derivatives of (7-Hydroxy-2-oxo-2*H*-chromen-4-yl)-acetic Acid Hydrazide, *Molecules*, 11, 134-147.
- M. El-Behery, H. El-Twigry (2007), Synthesis, magnetic, spectral, and antimicrobial studies of Cu(II), Ni(II) Co(II), Fe(III), and UO₂(II) complexes of a new Schiff base hydrazone derived from 7-chloro-4-hydrazinoquinoline. *Spectrochim. Acta Part A*, 66, 28-36.
- M.M. Woolfson (1980), 'An Introduction to X-ray Crystallography' Cambridge University Press Cambridge, 125-150.
- N.H. Al-Shaalan (2007), Antimicrobial activity and spectral, magnetic and thermal studies of some transition metal complexes of a Schiff base hydrazone containing a quinoline moiety. *Molecules*, 12, 1080-1091.
- N.H. Al-Shaalan (2011), Synthesis, Characterization and Biological Activities of Cu(II), Co(II), Mn(II), Fe(II), and UO₂(VI) Complexes with a New Schiff Base Hydrazone: *O*-Hydroxyacetophenone-7- chloro-4-quinoline Hydrazone. *Molecules*, 16, 8629-8645.
- N.P. Singh, V.P. Tyagi and B. Ratnam (2010), Synthesis and spectroscopic studies of tetradentate schiff base complexes of Cu(II), Ni(II), Mn(II) and Co(II), *J. Chem. Pharm. Res.*, 2(1), 473-477.
- N. Sirisoma, A. Pervin, H. Zhang, S. Jiang, J.A. Willardsen, M.B. Anderson, G. Mather, C.M. Pleiman, S. Kasibhatla, B. Tseng, J. Drewe and S.X. Cai (2009), Discovery of N-(4-methoxy phenyl)-*N*,2-dimethylquinazolin-4-amine, a potent apoptosis inducer and efficacious anticancer agent with high blood brain barrier penetration. *J. Med. Chem.* 52, 2341-2351.
- O. Kenichi, Y. Yoshihisa, O. Toyonari, I. Toru and I. Yoshio (1985), Studies on 4(1*H*)-Quinazolinones. 5. Synthesis and Antiinflammatory Activity of 4(1*H*)-Quinazolinone Derivatives. *J. Med. Chem.* 28, 568-576.
- P.S.N.Reddy, and B.V.Agarwal, (1987) Synthesis and Characterization of New Schiff Base Complexes of 2-Pyridinecarboxaldehyde and Thiosemicarbazides, *Syn. React. Inorg. Metal-Org. Chem.*, (17)6, 585 –594.
- P. Verhaeghe, N. Azas, M. Gasquet, S. Hutter, C. Ducros, M. Laget, S. Rault, P. Rathelot and P.Vanelle,(2008), Synthesis and antiplasmodial activity of new 4-aryl-2-trichloromethyl quinazolines. *Bioorg. Med. Chem. Lett.* 18, 396–401.
- P. Verhaeghe, N. Azas, S. Hutter, C. Castera-Ducros, M. Laget, A. Dumètre, M. Gasquet, J.P. Reboul, S. Rault, P. Rathelot, and P. Vanelle (2009), Synthesis and in vitro antiplasmodial evaluation of 4-anilino-2-trichloromethylquinazolines. *Bioorg. Med. Chem.* 17, 4313–4322.
- R.K. Agarwal, D. Sharma, L. Singh, and H. Agarwal (2006), Synthesis, Biological, Spectral, and Thermal Investigations of Cobalt(II) and Nickel(II) Complexes of *N*- Isonicotinamido -2,4-dichlorobenzalaldimine. *Bioinorg. Chem. and Appl.* Article ID 29234, 1–9.

- R. Saxena, Sahadev and S. Ahmad (2010), Synthesis and characterisation of transition metal complexes of 2,6-diacetylpyridine bis(S-methyl isothiosemicarbazone), *Oriental J. Chem.* 26(4), 1507-1511.
- R.S. Giri, H.M. Thaker, T. Giordano, J. Williams, D. Rogers, V. Sudersanam, and K.K. Vasu (2009), Design, synthesis and characterization of novel 2-(2,4-disubstituted-thiazole-5-yl)-3-aryl-3H-quinazolin-4-one derivatives as inhibitors of NF- κ B and AP-1 mediated transcription activation and as potential anti-inflammatory agents. *Eur. J. Med. Chem.* 44, 2184-2189.
- R.T. Vashi and C.D. Shelat (2010), Synthesis, Characterization and Antifungal activity of 2[4(2,3Dichlorophenyl)piperazine1yl)methyl]3[8hydroxyquinoline5yl]3(H)quinazolin-4-one ligand and its metal chelates. *Int. J. Chem. Res.* 1(2), 1114.
- R.T. Vashi, S.B. Patel and H.K. Kadiya (2010), Synthesis, Characterization and Biological Investigations on Metal Chelates of 2-[(8-hydroxyquinolinyl)-5-aminomethyl]-3-(4-chlorophenyl)-3(H)-quinazolin-4-one, *International J. Chem.Tech. Research*, 2(2), 1106-1111.
- S.H. Rekha, B.R. Patil, D.S. Badiger, R.S. Vadavi, K.B. Gudasi (2010), 2D Hector studies of 1,2-dihydroquinazolinone derivative: Synthesis characterization and anti-microbial study of its transition metal complexes. *Der. Pharma. Chemica*, 2(2), 116-128.
- S. Joshi, V. Pawar and V. Uma (2011), Antibacterial and Antioxidant Properties of Mn(II), Co(II), Ni(II) and Zn(II) Complex of Schiff base derived from Cephalexin. *Research J. Pharm. Biol. and Chem. Sci.* 2(1), 61-70.
- S.K. Sahu, Md. Afzal Azam, B.M. Banerjee, S. Achary, C. C. Behera and S. Sic (2008), Synthesis, Characterization and Biological Activity of 2-Methyl-3- aminoquinazolin-4(3H)-ones Schiff Bases, *J. Braz. Chem. Soc.* 19(5), 963-970.
- V. Alagarsamy, G. Muruganathan and R. Venkateshperumal (2003), Synthesis, Analgesic, Anti-inflammatory and Antibacterial Activities of Some Novel 2-Methyl-3- substituted Quinazolin-4-(3H)-ones, *Biol. Pharm. Bull.* 26(12), 1711-1714.
- V. Segarra, M.I. Crespo, F. Pujol, J. Belata, T. Domenech, M. Miralpeix, J. M. Palacios, A. Castro and A. Martinez, (1998) Phosphodiesterase inhibitory properties of losartan. design and synthesis of new lead compounds. *Bioorg. Med. Chem. Lett.*, 8, 505-510.
- W.J. Geary (1971), "The use of conductivity measurements in organic solvents for the characterisation of coordination compounds," *Coordination Chemistry Reviews*, 7(1), 81-122.
- X.X. Zeng, R.L. Zheng, T. Zhou, H.Y. He, J.Y. Liu, Y. Zheng, A.P. Tong, M.L. Xiang, S.R. Song, S.Y. Yang, L.T. Yu, Y.Q. Wei, Y.L. Zhao and L. Yang (2010), Novel thienopyridine derivatives as specific anti-hepatocellular carcinoma (HCC) agents: synthesis, preliminary structure-activity relationships, and in vitro biological evaluation. *Bioorg. Med. Chem. Lett.* 20, 6282-6285.
- Y. Kabri, A. Gellis and P. Vanelle (2009), Microwave-assisted synthesis in aqueous medium of new quinazolinone derivatives as anticancer precursors. *Green Chem.* 11, 201-208.
- Y. Kabri, N. Azas, A. Dumetre, S. Hutter, M. Laget, P. Verhaeghe, A. Gellis and P. Vanelle (2010), Original quinazolinone derivatives displaying antiplasmodial properties. *Eur. J. Med. Chem.* 45, 616-622.
- Y. Xia, Z.Y. Yang, M.J. Hour, S.C. Kuo, P. Xia, K.F. Bastow, Y. Nakanishi, P. Nampoothiri, T. Hackl, E. Hamel and K.H. Lee (2001), Antitumor Agents. Part 204: Synthesis and Biological Evaluation of Substituted 2-Aryl Quinazolinones. *Bioorg. Med. Chem. Lett.*, 11, 1193-1196.