Journal of Pharmaceutical and Medicinal Research 2(2) (2016) 52–54

ISSN: 2455-0280

Contents List available at JACS Directory

Journal of Pharmaceutical and Medicinal Research

journal homepage: www.jacsdirectory.com/jpmr

Mn(II) Complex of 4-((3-ethoxy-2-hydroxybenzylidene)amino)-N-(pyridine-2-yl)benzene sulfonamide: Synthesis, Characterization and Biological Evaluation

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ARTICLE DETAILS

Article history:
Received 29 May 2016
Accepted 09 June 2016
Available online 18 June 2016

Keywords:
Sulpha Pyridine
Novovanillin
Antimicrobial Activity

ABSTRACT

A novel $[Mn(L_2)_2Cl_2]$ complex with Schiff base 4-((3-ethoxy-2-hydroxybenzylidene) amino)-N-(pyridin-2-yl)benzenesulfonamide (L_2) has been synthesized and characterized by elemental analysis, magnetic moment, conductivity measurement, IR, electronic, powder XRD and EI mass spectra. In the present work it has been found that the azomethine nitrogen atom and phenolic oxygen atom of the Schiff base take part in coordination. The $[Mn(L_2)_2Cl_2]$ complex has been screened for *in vitro* antimicrobial activities.

1. Introduction

Addition of an amine to a compound containing a carbonyl functional group aldehyde or ketone, produces Schiff base. The resulting Schiff base can be an effective coordinating ligand if it bears an additional group usually a hydroxyl group near the site of condensation. A Schiff base can acts as a ligand because it usually contains -N and -O donor atoms [1]. The azomethine linkage is a significant feature that makes Schiff base ligands interesting for biological activity as well as chelation with metal ions [2]. Transition metal Schiff base complexes play very vital role as they are known to possess biological activities such as anticonvulsant, antibacterial, antiviral and antidiabetic [3]. Manganese plays essential roles in many metabolic and nonmetabolic regulatory functions [4] such as bone mineralization, connective tissue formation, energetic metabolism, enzyme activation, immunological and nervous system activities, reproductive hormone regulation and blood clotting.

Sulfonamides are well-renowned for their antibacterial [5, 6], antitumour [7], diuretic [8], and antithyroid [9] activities. Keeping in view of the pronounced biological activity of the metal complexes of Schiff bases derived from sulpha drugs, it was thought of worthwhile to synthesise and characterize Mn(II) with Schiff base 4-((3-ethoxy-2-hydroxybenzylidene) amino)-N-(pyridin-2-yl)benzenesulfonamide derived from sulphapyridine and Novovanillin(3-ethoxysalicylaldehyde). The antimicrobial activity of the $[Mn(L_2)_2Cl_2]$ has been investigated against *Pseudomonas aeruginosa, E. coli, Staphylococcus aureus, Aspergillus niger* and *Mucor sp*.

2. Experimental Methods

2.1 Measurements and Reagents

Melting point was determined using Elico melting point apparatus. Elemental analysis (C, H, N, S) were performed using elemental analyser. The percentage of metal was determined in ICP Atomic Emission Spectrometer - Thermo Electron IRIS INTREPID II XSP DUO make, with spectral range 165 to >1000 nm. Conductivity measurement for the complex was carried out using Elico conductivity bridge and dip type conductivity cell. IR spectrum of the complex was recorded in KBr pellets with Perkin Elmer IR RXI Spectrometer in the 4000-400 cm^{-1} range. The electronic spectrum was recorded in Perkin Elmer Lambda 35 spectrometer in the 190-1100 nm range. Magnetic susceptibility was determined using Gouy method-PICO make. The Powder XRD was recorded in Shimadzu Model60000 instrument with Cu Kα radiation (λ =1.54060) from a Cu target. Sulphapyridine was purchased from HIMEDIA and Novovanillin was purchased from Sigma Aldrich. Solvents like DMF and DMSO were purchased from E Merck and used without further purification. $MnCl_2.4H_2O$ salt used was of AR grade (AR Glaxo Chemicals). Commercial ethanol was dried over anhydrous quicklime for 24 hours, filtered and distilled before use.

2.2 Synthesis

2.2.1 Synthesis of Schiff Base 4-((3-Ethoxy-2-Hydroxybenzylidene) Amino)-N-(Pyridin-2-Yl)Benzenesulfonamide(L_2)

The synthesis, chemistry and antimicrobial activity of this Schiff base has been followed as per our previously published report [10].

2.2.2 Synthesis of $[Mn(L_2)_2Cl_2]$ Complex

To a hot magnetically stirred ethanolic solution of Schiff base (0.796 g, 0.002 mol) in minimum quantity of dimethyl formamide, an ethanolic solution of the manganous (II) chloride tetrahydrate (0.197 g, 0.001 mol) was added. The mixture was refluxed for 5 hrs on a water bath. The precipitate formed during refluxing was cooled in an ice bath and collected by suction filtration, washed thoroughly with ethanol and pet ether and dried. The pale yellow colour solid obtained was mostly insoluble in some common organic solvents and soluble in polar solvents like DMF and DMSO.

2.2.3 Antimicrobial Susceptibility Test by Disc Diffusion Technique

Disc impregnated with known concentration of antibiotic was placed on agar plate that has been inoculated uniformly over the entire plate with culture of the bacterium to be tested. The plate was incubated for 18-24 hrs at 310 K for bacteria and 24-48 hrs at 298 K for fungi. During this period, the antimicrobial agent diffuses through the agar and may prevent the growth of the organism. Effectiveness of susceptibility is proportional to the diameter of zone of inhibition. The diameter of the zone of inhibition (mm) of growth was measured.

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Cite this Article as: V. Gomathi, R. Selvameena, Mn(II) complex of 4-((3-ethoxy-2-hydroxybenzylidene)amino)-N-(pyridine-2-yl)benzenesulfonamide: synthesis, characterization and biological evaluation, J. Pharm. Med. Res. 2(2) (2016) 52–54.

3. Results and Discussion

3.1 Analytical Data

The yield and M.pt. for the complex are 60% and 280 °C. The elemental analysis for the complex: Calcd (%); C (52.18), H (4.13), N (9.13), S (6.95), Mn(5.97), Cl(7.71); Found(%) C (52.68), H (4.09), N (9.54), S (6.43), Mn (5.22), Cl (7.40). The elemental analysis results indicate metal: ligand stoichiometry of 1:2 for this complex. The molar conductance of the Mn (II) complex is 12.48 ohm^{-1}cm^2 mol^{-1} indicates nonelectrolytic nature and the chloride ions are present inside the coordination sphere.

3.2 Infrared Spectral Data

A sharp band in the IR spectrum (Fig. 1) at 1627 cm^{-1} is assignable to the azomethine ν(-CH=N) present in the Schiff base L_2 that undergoes a shift to lower frequency 1597 cm^{-1} indicates coordination of azomethine nitrogen [11, 12] with Mn(II) ion in the complex. This is further reflected by the non-ligand band observed in the complex at 440 assignable to ν (M-N) [13]. The coordination through phenolic oxygen, is revealed by the appearance of ν (O-H) mode in the complex is almost in the same region as Schiff base suggests the coordination of ν (O-H) without deprotonation. The coordination of phenolic oxygen is further confirmed by the appearance of the non-ligand band at 526 cm^{-1} due to *ν* (M-O) in the complex [14]. The advent of new band in the far-IR spectra (Fig. 2) in the region 313-318 cm^{-1} is assigned to the ν(M-Cl) mode in the complex confirms the coordination of chlorine with the central metal ion [15].

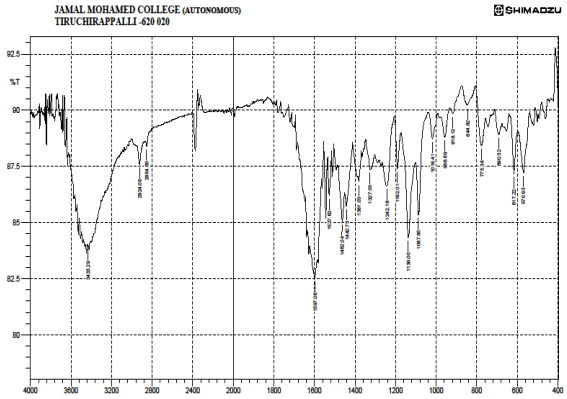

Fig. 1 IR spectrum of $[Mn(L_2)_2Cl_2]$

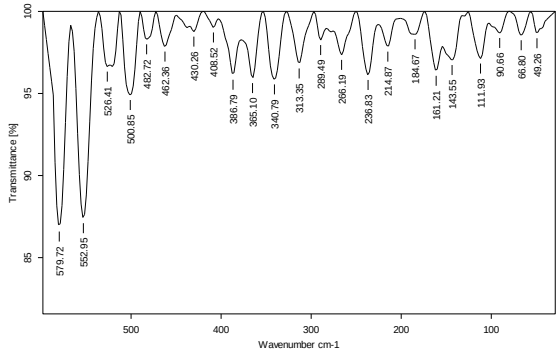

Fig. 2 Far IR spectrum of $[Mn(L_2)_2Cl_2]$

3.3 Electronic Spectral Analysis and Magnetic Susceptibility Measurement

The Mn(II) complex exhibits band at 520 nm due to $^6A_{1g} \rightarrow {}^4T_{1g}(G)$ transition [16] and has a magnetic moment value of 5.90 B.M suggesting octahedral geometry.

3.4 Powder XRD Spectra

The powder XRD spectrum of Schiff base ligand L2 was compared with the spectrum of the Mn(II) complex (Fig. 3 and Table 1). Few new peaks appear in the spectrum of complex compared to the spectrum of the ligand which indicates the formation of metal chelates. The size DXRD of the Schiff base and complex are calculated with the help of XRD patterns using Debye Scherrer's formula [17].

$$D_{XRD} = 0.9\lambda/\beta \cos\theta$$

Where 'λ' is the wavelength, 'β' is the full width at half maximum and 'θ' is the peak angle. The Schiff base and the complex have the crystallite size of 73 and 38 nm respectively, suggest that Schiff base and its complex are nanocrystalline. The geometry of the complex has been supported from 2θ, interplanar d-spacing and Miller indices (h, k, l) values. The unit cell calculations have been done for cubic symmetry from the important peaks and ($h^2+k^2+l^2$) values were determined for the complex. The Miller indices for complex are 1, 7, 11, 12, 17, 24, 29, 37, 51, 70, 83, 102 and 146. The presence of forbidden number 7 indicates that the Mn(II) complex may belong to the hexagonal or tetragonal systems. The analytical and the spectral data confirms Mn(II) complex to be a hexagonal system.

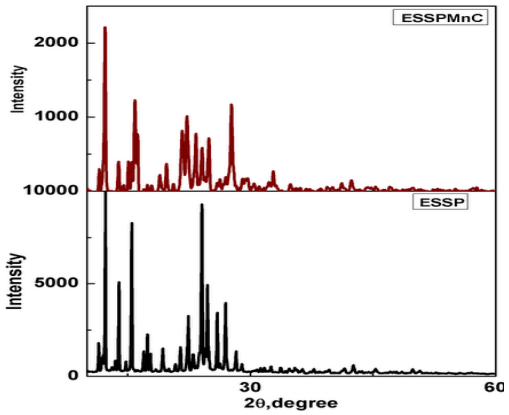

Fig. 3 Powder XRD pattern of $[Mn(L_2)_2Cl_2]$

Table 1 Powder XRD data of $[Mn(L_2)_2Cl_2]$

Peak No.	Relative Intensity (%)	d-spacing (Å)	2θ(°)	θ(°)	Sin θ	Sin^2 θ	1000 sin^2 θ	1000 sin^2 θ / CF ($h^2+k^2+l^2$)	(hkl)
1	2.42	4.4321	4.5264	2.2632	0.0394	0.005159	1.559	1.00	100
2	100.00	7.2404	12.224	6.1123	0.1064	0.011332	11.3320	7.27	-
3	17.93	5.8816	15.063	7.5312	0.1310	0.017179	17.1790	11.02	311
4	55.49	5.5762	15.893	7.9470	0.1382	0.019115	19.1150	12.26	320
5	9.83	4.6997	18.883	9.4415	0.1640	0.026909	26.9090	17.26	410
6	45.73	4.0019	22.214	11.107	0.1926	0.037110	37.1100	23.80	422
7	26.61	3.5690	24.949	12.474	0.2160	0.046656	46.6560	29.93	521
8	53.39	3.2222	27.685	13.842	0.2392	0.057241	57.2410	36.72	610
9	12.28	2.7308	32.797	16.398	0.2823	0.079705	79.7050	51.13	551
10	1.46	2.3295	38.653	19.326	0.3309	0.109535	109.5350	70.26	653
11	6.24	2.1349	42.337	21.168	0.3611	0.130400	130.0400	83.41	911
12	2.71	1.9309	47.063	23.531	0.3992	0.159409	159.4090	102.25	772
13	1.22	1.6124	57.076	28.538	0.4777	0.228245	228.2450	146.41	981

3.5 EI Mass Spectra

The complex shows the m/z peak which corresponds to the base peak in mass spectrum. m.wt. calcd. 919.84 found 919.99. The peak support the formula assigned to the complex and confirm the stoichiometry of metal chelate as type $[M(L_2)_2\,Cl_2]$. The molecular ion peak is in good agreement with the suggested molecular formula indicated from elemental analysis.

Based on these evidences, structure has been proposed for the Mn(II) complex as shown in Fig. 4.

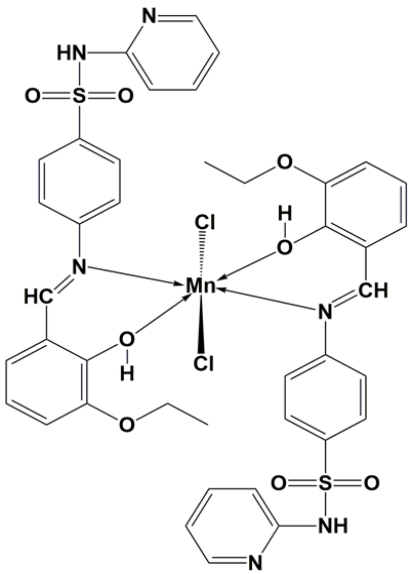

Fig. 4 Structure of $[Mn(L_2)_2Cl_2]$

3.6 In-Vitro Antimicrobial Bioassay

The antibacterial activity of $[M(L_2)_2 Cl_2]$ complex was tested against gram positive bacterial species *Staphylococcus aureus*, gram negative bacterial species *E. coli* and *Pseudomonas aeruginosa* (Fig. 5) and fungal species *Aspergillus niger* and *Mucor sp* (Fig. 6) by disc diffusion method [18]. The test was carried out in DMSO solution at a concentration of 100 ppm. The results were compared with standard drugs Ciprofloxacin for bacteria and Nystatin for fungi at the same concentration. The bio potency of the complex has been much pronounced compared to the free Schiff base. The enhanced activity of the complex can be explained on the basis of Overtone's concept [19] and Tweedy's Chelation theory [20].

Fig. 5 In *vitro* antibacterial screening of $[Mn(L_2)_2Cl_2]$ against *Staphylococcus aureus, E.coli* and *Pseudomonas aeruginosa*

Fig. 6 In *vitro* antifungal screening of $[Mn(L_2)_2Cl_2]$ against *Aspergillus niger* and *Mucor sp*

4. Conclusion

The $[Mn(L_2)_2Cl_2]$ complex in combination with bidentate Schiff base have been synthesized and characterized. Satisfactory analytical and spectral studies reveal that the Schiff base coordinate to metal ion via azomethine nitrogen and hydroxyl oxygen, two chlorine atoms are coordinated to the metal ion, the complex is nonelectrolytic in nature and confirms the octahedral geometry of this complex. The result of antimicrobial activity indicates that the Mn(II) complex has remarkable activity against bacterial and fungal species. The $[Mn(L_2)_2Cl_2]$ complex has higher antifungal activity against *Mucor sp* when compared to other fungal and bacterial species.

Acknowledgement

The authors are grateful to the Management, Seethalakshmi Ramaswami College, Tiruchirappalli.

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