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Synthesis, Characterization and Antimicrobial Study of Some 3d Metal Complexes of Sulfadoxine

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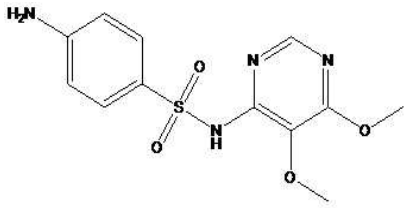
Abstract: Sulfadoxine complexes of Mn(II), Co(II), Ni(II) and Cu(II) metal chlorides were synthesized and characterized by elemental analysis, molar conductivity, magnetic susceptibility measurement, Infrared (IR)and Ultraviolet (UV) spectroscopy and antimicrobial activity. Some physical parameters were obtained using molar conductance measurement and melting point determination. Based on the analytical and spectroscopic data, the complexes were proposed to havethe formula ML_2Cl_2. (L = Sulfadoxine) .The spectroscopic data propose that sulfadoxine co-ordinated through (N-H) and (O=S=O) making it a bidentate ligand. Ligand and metal complexes are screened for their antibacterial activity.
Keywords: Sulfadoxine,Transition Metals,Spectroscopic Techniques,Antibacterial Activity.

1. Introduction

Sulfadoxines are among the most widely used antibacterial agents in the world, chiefly because of their low cost, low toxicity and excellent activity against bacterial diseases.Sulfadoxine is an ultra long lasting blood schizonticidal sulfonamide,used in combination with pyrimethamine in the prophylaxis and treatment of malaria caused by chloroquine resistant strains of plasmodium falciparum.[1-4]

Vector borne diseases are rapidly spreading in the tropical and subtropical regions. Although many chemotherapeutic agents are in the market; there is tremendous increase in the ability of parasite to survive or multiply despite the administration and absorption of drugs. This is generally accepted to be initiated primarily through a spontaneous mutation that reduces level of sensitivity of the drug. Antimicrobial resistance is fast becoming a global concern with rapid increase in the multidrug resistance in bacteria. Thus some previously treatable pathogens are now becoming untreatable. Compounds containing pyrimidine ring have been reported to possess biological activities.Many therapeutic agents containing pyrimidine ring which enable them to coordinate with metal ion in the body system. Transition metal ions are responsible for the proper functioning of different enzymes. In our effort to search for novel chemotherapeutic drugs against parasitic diseases, we reported the synthesis, characterization and antimicrobial study of Mn(II), Co(II), Ni(II) and Cu(II) complexes of sulfadoxine.



: 4-Amino-*N*-(5,6-dimethoxy-4-pyrimidinyl)benzenesulfonamide

Figure 1: Structure of Sulfadoxine

2. Experimental

2.1 Materials and Physical Measurement:

All chemicals used were of Analytical grade. Pure sample of sulfadoxine having molecular formula, $C_{12}H_{14}N_4O_4S$ and molecular weight 310.33 g/mol was obtained from pharmaceutical company. Metal salts were of Merck Chemicals. Melting points were taken in open capillaries on a melting point apparatus. UV spectra were recorded in the range 200 - 800 nm on Perkin Elmer UV Spectrometer by making solutions in Dimethyl Sulfoxide (DMSO). The IR spectra were recorded as KBr pellets in range 4000-400cm^{-1}on Shimadzu FTIRsystem. Carbon, Hydrogen and Nitrogen were determined on thermo Fisher Flash Elemental Analyzer. Magnetic moment was carried out by Gouy balance. Conductivity was measured by making solutions in DMSO.

2.2 Synthesis of Complexes:

1.5 g(4mM) of sulfadoxinein 20mLwas dissolved in ethanol. 2mM of each metal salt wasdissolved in ethanol. The reaction mixture was refluxed for 3hours, after adjusting pH.The solution was allowed to cool to room temperature and left to dry. The crystals were filtered, washed thrice with ethanol and dried in desiccator containing calcium chloride as drying agent.

2.3 Antibacterial Screening:

Agar well Diffusion Method:

7g of nutrient agar was weighed into a 250 mL conical flask. 250mL distilled water (sterilized for 24hours) was mixed with agar and it was covered properly with cotton wool and foil paper so as to avoid contamination. The solution was then heated for 15minutes so as to dissolve the nutrient agar. It was sterilized for 24hours in an autoclave. The nutrient agar was then introduced into the petridish and was allowed to set properly. 1cm hole was bored at the center of the plate with the aid of hole borer and was allowed to remove the cracked hole so as to view the bottom of the petridish. This was left in incubator for 24hours to allow the outgrowth of microorganisms. The zone of inhibition of complexes and ligand was determinedin mm. DMSO was used as control. The bacterial species against *Escherichia coli (E. coli), Staphylococcus aureus (S. aureus), Bacillus Subtilis (B. Subtilis)* and *BacillusMegaterium (B. Megaterium)*were used as test organisms.

3. Results and Discussion:

The synthesized complexes are stable solids. They are soluble in DMSO. Analytical data and conductometric studies as shown in Table 1 suggest 1: 2 [M: L] ratio.C, H and N analyses with metals are given in Table 2. Measured conductance values of these complexes are too low to account for their electrolyticbehavior.

Table 1: Analytical Data of Complexes

Sr. no.	Composition of Complex	Colour	% Yield	M.P (°C)	Magnetic Moment (B.M.)	Molar Conductance $\Omega^{-1}cm^2mol^{-1}$
1	$C_{12}H_{14}N_4O_4S$	White		191	-	14.55
2	$Mn[C_{12}H_{14}N_4O_4S]_2Cl_2$	White	72	195	5.24	11.08
3	$Co[C_{12}H_{14}N_4O_4S]_2Cl_2$	Light Pink	68	205	4.87	12.1
4	$Ni[C_{12}H_{14}N_4O_4S]_2Cl_2$	Pistal green	58	166	3.06	10.9
5	$Cu[C_{12}H_{14}N_4O_4S]_2Cl_2$	Light Brown	61	200	1.94	11.00

Table 2: Analysis of SulfadoxineComplexes

Compound	% Cfound(calc.)	%H found(calc.)	N%found(calc.)	M%found(calc.)
Sfd(sulfadoxine)	46.17(46.44)	4.01(4.22)	18.03(18.06)	-
$Mn(Sfd)_2Cl_2$	38.60(38.60)	3.51(3.75)	14.99(15.03)	7.20(7.390
$Co(Sfd)_2Cl_2$	38.35(38.43)	3.02(3.7)	16.23(16.27)	7.75(7.86)
$Ni(Sfd)_2Cl_2$	38.39(38.44)	3.62(3.73)	14.86(14.94)	7.78(7.83)
$Cu(Sfd)_2Cl_2$	38.11(38.19)	3.63(3.71)	14.73(14.85)	8.36(8.42)

Table 3: UV Spectra Assignments for Sulfadoxine and its Complexes

Compound	Wavelength in nm	Wavelength in cm^{-1}	Assignment
Sfd (Sulfadoxine)	202	49505	Π-Π *
	271	36900	n-Π *
$Mn(Sfd)_2Cl_2$	375	26666	n-Π *
	410	24691	MLCT
$Co(Sfd)_2Cl_2$	452	22124	$^4T_1g \rightarrow {}^4T_1g(p)$
	534	18692	$^4T_1g \rightarrow {}^4A_1g$
	575	17391	$^4T_1g \rightarrow {}^4T_2g$
$Ni(Sfd)_2Cl_2$	425	23529	$^3A_2g \rightarrow {}^3T_1g(p)$
	450	22222	$^3A_2g \rightarrow {}^3T_1g$
	550	18182	$^3A_2g \rightarrow {}^3T_2g$
$Cu(Sfd)_2Cl_2$	830	12048	$^2Eg \rightarrow {}^2T_2g$

3.1Electronic spectra of Ligand and Complexes

The electronic spectra of sulfadoxine and its metal complexes are presented in the Table. 3. The electronic spectrum of sulfadoxine in DMSO gave absorption at 202 nm and 271 nm, the bands assigned to Π-Π */ n-Π *. No d-d transitions are expected in Mn(II). Transitions attributed to n-Π * and metal to ligand charge transfer occur at 375nm and 410 nm respectively.The electronic configuration of$Co(Sfd)_2Cl_2$isd^7 with spectroscopic ground state term ^4F.The complex showed three bands in visible region. The electronic configuration of $Ni(Sfd)_2Cl_2$is d^8 and its spectroscopic ground term ^3F. As expected, Cu(II) complex showed broad band at 830nm attributed to $^2Eg \rightarrow {}^2T_2g$.[5-7]

3.2 IR Spectra of complexes:

The important IR spectral bands of both ligand and complexes with their functional group are given in the Table.4. The absorption bands 3454 and 3241 cm^{-1} are assigned to N-H stretching vibration.[8-12]Similar bands are shifted to lower and higher wavelengths in the metal complexes, such changes clearly indicate that lone pair of NH_2 is involved in the complexation with metals, whereas the sulfoxide O=S=O stretching occurs at 1374$cm^{-1}$is also observed to shift to lower wavelengths thus sulfonyl oxygen is coordinated with metals.[13-15]The non-ligand bands in the range 592 - 678$cm^{-1}$are assigned to M-Cl bond. Hence in these complexes,sulfadoxine acts as bidentateligand coordinating through oxygen of sulfone group and nitrogen of amino group.[16-18]

The magnetic moment found for Mn(II), Co(II), Ni(II) and Cu(II) are 5.24, 4.87, 3.06 and 1.94 B.M. respectively, these values suggest octahedral geometry which is in good agreement with the data of electronic spectra as given in Table.3.

Table 4: Selected IR (cm^{-1}) Assignments for Sulfadoxine and its Complexes

Ligand/ Complexes	νNH_2 a sym,sym	ν C=N	νO=S=O sym	ν M-X
Sfd (Sulfadoxine)	3454, 3241	1654	1374	-
$Mn(Sfd)_2Cl_2$	3465, 3240	1647	1319	639
$Co(Sfd)_2Cl_2$	3377,3238	1650	1305	592
$Ni(Sfd)_2Cl_2$	3464,3263	1648	1318	674
$Cu(Sfd)_2Cl_2$	3359,3268	1598	1320	678

Table 5:Antibacterial activity Zone of Inhibition in,mm.

Compound	***Escherichia coli***	***Bacillus subtilis***	***Bacillus megaterium***	***Staphylococcus aureus***
Sfd (Sulfadoxine)	13.10	13.14	-	11.20
$Mn(Sfd)_2Cl_2$	12.30	16.80	16.50	13.10
$Co(Sfd)_2Cl_2$	15.20	12.10	11.10	12.60
$Ni(Sfd)_2Cl_2$	-	14.10	14.40	6.80
$Cu(Sfd)_2Cl_2$	15.10	13.20	11.20	11.02
DMSO(control)	0	0	0	0

4. Conclusion

We report the synthesis, characterization and antimicrobial studies of Mn(II), Co(II), Ni(II) and Cu(II) complexes of sulfadoxine. The complexes formulated as (ML_2Cl_2) are six coordinated complexes consist of two molecules of sulfadoxine and two chloride ions. The complexes were characterized by elemental analysis, electronic and IR spectroscopy. Spectroscopic analyses confirmed the coordination of drug through amide nitrogen and oxygen of sulfone group. The antibacterial screening of complexes showed varied activities.

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