



Synthesis and Characterization of Some Metal (II) Complexes of Sulfadoxine

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Abstract The studies and manipulations of the coordination chemistry of bioactive organic ligands has been a promising means of pharmaceutical innovations. In this study, metal (II) complexes of sulfadoxine (SDX) were synthesized and characterized by physicochemical, IR and electronic spectroscopies. The complexes were formulated as $[M(SDX)_2(H_2O)_2]$ ($M = Cd(II)/Cu(II)/Zn(II)$), $[M(SDX)_2Cl_2]$ ($M = Ni(II)/Co(II)/Mn(II)$). They were insoluble in water, which is an indication of covalent and non-electrolytic character. Their spectroscopic data indicated that sulfadoxine ligand acted as a bidentate chelating agent showing a coordination either via the pyrimidine nitrogen and the nitrogen of the SO_2NH moiety as in the case for Cu(II), or via the pyrimidine nitrogen and the amino nitrogen of the terminal NH_2 group as in the case for Ni(II), Cd(II), and Co(II). The complexes formed are inferred to assume a six coordinate octahedral geometry while Zn(II) and Mn(II) complexes exhibit tetrahedral geometry. The successful synthesis and characterization of these complexes therefore presents a new bioactive substance with virgin pharmaceutical potentials.

Keywords Sulfadoxine, synthesis, Metal(II) complexes, complexes geometry

Introduction

The biological activity of sulpha drugs as well as the ligands derived from them has been known for a long time, and their activities has been reported to increase on complexation with metal ions [1]. This is true as the resultant structural changes that normally occur on complexation with the metal, center alters and sometimes improve the activities of the substance [1-3]. A number of references are now available to show that the condensation products of sulpha drugs with aldehydes, ketones or their derivatives are biologically very active. Besides having good complexing ability, their metal complexes play important roles in metabolic and toxicological function in biological systems through exchanges of different functional groups without modification of the structural features [4-7]. The increased activity includes; anti-tumor [8, 9], anti-angiogenic [10], anti-tubercular [11], anti bacteria and anti fungal [12-17]. One of the most interesting features of drug-metal coordinated system is the concerted spatial arrangement of the drug (ligands) around the metal ion [18].

In this work, complexes of sulpha drug are synthesized using such divalent metals as Cu(II), Ni(II), Co(II), Zn(II), Mn(II) and Cd(II). This is however aimed at the production of new bioactive substances with exploitable pharmaceutical potentials

Material and Methods

All Solvents were obtained from Aldrich and BDH in analytical grade. They were used without further purification. The Ligand (sulfadoxine) was obtained from Bond Pharmaceutical Industry Limited, Awe Oyo State, Nigeria. FT-IR spectra was obtained as KBr discs on a Parkin-Elmer BX spectrophotometer in the range $4000-250cm^{-1}$. Solid reflectance of the ligand and the complexes were run neat (without solvent) using GENESYS 10S V1 spectrophotometer. Melting point was determined using Gallenkamp melting point apparatus made in England.



Synthesis of Complexes

The complexes are synthesized while adopting the method by Tella and Obaleye [19]. For $[\text{Cu}(\text{SDX})_2(\text{H}_2\text{O})_2]$ according to this method, alkaline solution of sulfadoxine (1.241g, 0.004moles) was added drop wise into an aqueous solution of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (0.499g, 0.002moles). The resulting mixture was stirred magnetically for two hours and was left to stand overnight protected from light. The precipitate formed was centrifuged, washed several times with distilled water and dried in a desiccator on silica gel. Likewise, other complexes including; $[\text{Ni}(\text{SDX})_2\text{Cl}_2]$, $[\text{Cd}(\text{SDX})_2(\text{H}_2\text{O})_2]$, $[\text{Co}(\text{SDX})_2\text{Cl}_2]$, $[\text{Mn}(\text{SDX})_2\text{Cl}_2]$ and $[\text{Zn}(\text{SDX})_2(\text{H}_2\text{O})_2]$ were synthesized using the aqueous solutions of their hydrated salts namely $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$, $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ and $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ respectively.

Melting point

The melting point of the ligand and the metal complexes was determined using Gallenkamp melting point apparatus made in England. Averages of triple determinations were recorded.

Electronic spectra

The solid reflectance spectra of the ligand and the complexes were run neat (without solvent) using GENESYS 10S V1 spectrophotometer.

Infrared spectra

In order to study the binding mode of sulphadoxine to metal in the complexes, infrared spectrum of the free ligand was compared with the spectra of the metal complexes. These were recorded neat as KBr pellets in Perkin-Elmer BX FT-IR spectrophotometer.

Results and Discussion

Table 1: Analytical Data for the Ligand and its Complexes

Compound	Colour	Formula Weight (g/mole)	%metal Found(Calc)	Melting point (°C)	%Yield
SDX	White	310.31	-	194-198	-
$[\text{Ni}(\text{SDX})_2\text{Cl}_2]$	Green	750.19	7.04(7.82)	350	76.0
$[\text{Cu}(\text{SDX})_2(\text{H}_2\text{O})_2]$	Brown	718.16	9.56(8.85)	350	67.8
$[\text{Cd}(\text{SDX})_2(\text{H}_2\text{O})_2]$	White	769.03	15.01(14.62)	350	44.3
$[\text{Co}(\text{SDX})_2\text{Cl}_2]$	Pink	750.43	7.01(7.85)	350	58.5
$[\text{Mn}(\text{SDX})_2\text{Cl}_2]$	Brown	746.46	7.82(7.36)	350	79.8
$[\text{Zn}(\text{SDX})_2(\text{H}_2\text{O})_2]$	White	722.04	10.61(9.06)	350	59.7

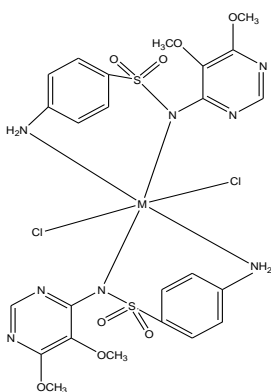


Figure 1: Proposed structure for $[\text{M}(\text{SDX})_2\text{Cl}_2]$ $M = \text{Co}, \text{Ni}, \text{Cd}$

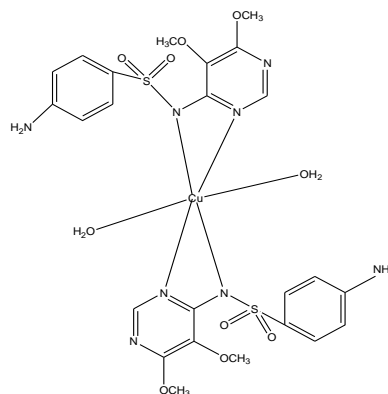


Figure 2: Proposed structure for $[\text{Cu}(\text{SDX})_2(\text{H}_2\text{O})_2]$

Table 2: Electronic Spectra of Sulfadoxine and its Metal Complexes

Complex/ligand	Wavelength (nm)	Frequency (cm^{-1})	Assignment	Tentative geometry
SDX	284	35211	n- π^* / π - π^* overlap	-

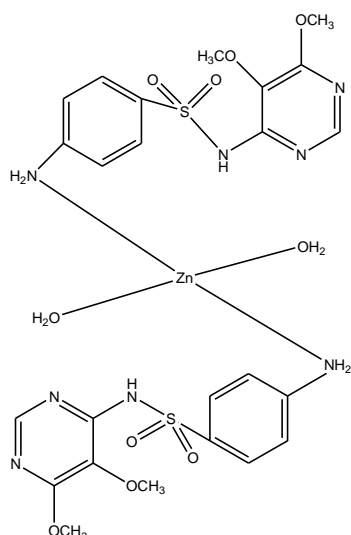
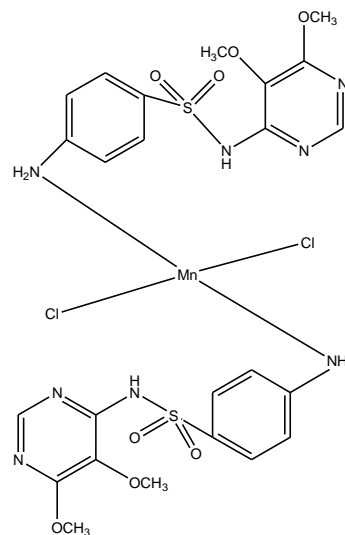


[Ni(SDX) ₂ Cl ₂]	296	33784	$\pi-\pi^*$	Octahedral
	467	21413	$^3A_{2g} \rightarrow$	
	550	18182	$^3T_{1g}(P)$	
			$^3A_{2g} \rightarrow$	
			$^3T_{1g}(F)$	
[Cu(SDX) ₂ (H ₂ O) ₂]	670	14925	$^2E_g \rightarrow ^2T_{2g}$	Octahedral
[Cd(SDX) ₂ (H ₂ O) ₂]	251	39841	MLCT	Octahedral
[Co(SDX) ₂ Cl ₂]	673	14861	$^4T_{1g} \rightarrow ^4T_{2g}(F)$	Octahedral
	510	19608	$^4T_{1g}$	
	448	22321	$\rightarrow ^4A_{2g}(F)$	
			$^4T_{1g} \rightarrow$	
			$^4T_{1g}(P)$	
[Mn(SDX) ₂ Cl ₂]	287	34843	$\pi-\pi$	Tetrahedral
[Zn(SDX) ₂ (H ₂ O) ₂]	249	40161	MLCT	Tetrahedral
	281	35587	$n-\pi^*$	

Table 3: Selected Infrared Bands (cm⁻¹) of Sulfadoxine and its Metal Complexes

Complexes/Ligand	νNH_2 Asym/Sym	νSO_2 Asym/ Sym	$\nu C=N$	$\nu S-N$	$\nu N-H(SO_2NH)$	$\nu M-N$	$\nu M-X$
SDX	3371s 3469s	1159s 1316s	1590s 1649s	846	3246s		
[Ni(SDX) ₂ Cl ₂]	3622b,w	1125s 1322m	1447b 1589m	851vs	-	566s	669m
[Cu (SDX) ₂ (H ₂ O) ₂]	3445b 3760m	1023m 1116s	1450s 1632s	849m	-	496s	
[Cd(SDX) ₂ (H ₂ O) ₂]	3423m 3611m	1125s	1441m 1584m	866m	-	450m 569m	
[Co(SDX) ₂ Cl ₂]	3446b 3691m 3760m	1110s	1553w 1649m		-	580m	
[Mn(SDX) ₂ Cl ₂]	3457b 3686m 3760m	1117	1461w 1583m 1640m	854w	-	515w	646m
[Zn(SDX) ₂ (H ₂ O) ₂]	3377m 3463m	1159s 1316s	1447s 1589s	840s	3240m	452m 552s	



Figure 3: Proposed structure for [Zn(SDX)₂(H₂O)₂]Figure 4: Proposed structure for [Mn(SDX)₂Cl₂]

Infrared Spectra of the Ligand and the Complexes

The infrared spectra (table 3) of the sulfadoxine ligand and those of the metal complexes were compared to determine the coordination sites that were involved in bonding. The spectra of the sulfadoxine ligand display two strong bands around 3371 cm⁻¹ and 3469 cm⁻¹ assigned to symmetric and asymmetric stretching modes of the terminal NH₂ group respectively. A single band observed around 3246 cm⁻¹ was assigned to ν_{N-H} vibration of the secondary amine attached to sulfonyl group of the ligand. A band around 846 cm⁻¹ was observed and assigned to S-N stretching vibration. Two bands observed at 1590 cm⁻¹ and 1649 cm⁻¹ were assigned to C=N stretching vibration [20]. The presence of SO₂ moiety in the ligand was confirmed by the appearance of two bands at 1159 cm⁻¹ and 1316 cm⁻¹ and were assigned to symmetric and asymmetric stretching modes respectively.

The formation of metal complexes can be confirmed from infrared spectra of the reported complexes which when compared with that of the free ligand provided information concerning the modes of coordination. The bands at 3371 cm⁻¹ and 3469 due to ν_{NH_2} were shifted to higher (red shift) wave number in all the complexes (3760 and 3445 cm⁻¹ for Cu(II), 3611 and 3423 cm⁻¹ for Cd(II), 3760, 3691 and 3446 cm⁻¹ for Co(II), 3463 and 3377 cm⁻¹ for Zn(II) complexes). Ni(II) showed only one band with respect to the ligand around 3622 cm⁻¹). The sharp bands at 3246 cm⁻¹ assigned to the vibration due to N-H of the SO₂NH group in the ligand was conspicuously absent or disappeared in the spectra of all the metal complexes except in Zn(II) as a result of deprotonation of the SO₂NH moiety. This further suggests or confirms the involvement of sulfonyl nitrogen in chelation forming Metal-Nitrogen bond.

These results indicate that the NH₂ group is involved in coordination, this is shown by additional band in Co(II) complex, a shift to higher wave number in Cd(II) and formation of a single band at 3622 cm⁻¹ in Ni(II). This observation confirm the coordination of Co(II), Ni(II) and Cd(II) ions through the terminal NH₂ (primary amine) attached to the benzene moiety of the ligand and also through the nitrogen of the SO₂NH moiety. The peak observed around 1590 cm⁻¹ is assigned to C=N stretching vibration in the free sulfadoxine ligand, the peak shifted to a lower wave number by about 1450 cm⁻¹ in Cu(II) complex indicating the coordination of Cu(II) ion to the pyrimidine nitrogen [19]. The infrared data reveal that the Cu(II) ion coordinated through the pyrimidine nitrogen and the nitrogen of the SO₂NH moiety. For Zn(II), all the bands remain almost in the same position with a little shift in the NH₂ band when compared with that of the ligand, indicating the coordination of the zinc ion only through the NH₂ group. For Mn(II) there was a shift and additional band for NH₂ group. The observation of new bands around 450-689 cm⁻¹ in the far infrared is assigned to M-N and M-X stretching. This was further an evidence of coordination.

Electronic spectra

The electronic spectra data of the ligand and its complexes were used for assigning the stereochemistry of the metal complexes based on the positions and number of *d-d* transition peaks. This was recorded neat (solid reflectance) in the range 200-800 nm of the spectrum using Genesys 10s spectrophotometer. The electronic spectra of the ligand showed a band in the region 200-400 nm with λ_{max} at 284 nm (35211 cm⁻¹) assigned to $n-\pi^*/\pi-\pi^*$ overlap [21]. The appearance of additional band in the metal complexes as compared to one band in the ligand indicates the overlap of



d-orbital of metal atom to the p-orbital of the ligand and that confirms complex formation. Extra bands were observed in Ni(II), Co(II) and Cu(II) complexes which have been attributed to d-d bands. Ni(II) is a d^8 system and therefore will have a 3F ground term with a singlet (an A_{2g}) most stable ground state. In an octahedral field therefore, we expect three transitions. Three transitions were observed in the spectra of Ni(II) at 296 nm (33784 cm^{-1}) assigned to $\pi-\pi^*$, 467 nm (21413 cm^{-1}) assigned to $^3A_{2g} \rightarrow ^3T_{1g}(P)$ transition, and 550 nm (18182 cm^{-1}) assigned to $^3A_{2g} \rightarrow ^3T_{1g}(F)$; the lowest transition $^3A_{2g} \rightarrow ^3T_{2g}$ transition was not observed. Co(II) is a d^7 system with a 4F ground term and a triplet most stable ground state. The three transitions were observed in Co(II) complex at 673 nm (14861 cm^{-1}) assigned to $^4T_{1g} \rightarrow ^4T_{2g}(F)$, 510 nm (19608 cm^{-1}), assigned to $^4T_{1g} \rightarrow ^4A_{2g}(F)$ and 448 nm (22321 cm^{-1}) assigned to $^4T_{1g} \rightarrow ^4T_{1g}(P)$ transition. Mn(II) is a d^5 system, Cd and Zn are d^{10} systems so no d-d band were observed in their complexes this is because the 3d and 4d (as in the case for Zn(II) and Cd(II) respectively) orbital is either partially filled (as in case for Mn(II)) or fully filled (as for Cd and Zn). A charge transfer band from metal to ligand is expected in these complexes. However a metal to ligand charge transfer band was observed in the spectra of Zn(II) complex at 249 nm (40161 cm^{-1}). For Mn(II) a band at 34843 nm (34843 cm^{-1}) was observed and assigned to $\pi-\pi^*$.

Conclusion

It is established from our result and the previous reports that Sulfadoxine ligand coordinates effectively with the metal centers. The ligand showed a bidentate coordinating nature to the metal centers, where it coordinated through either the pyrimidine nitrogen atom and sulfonyl nitrogen atom or through the sulfonyl nitrogen atom and amino nitrogen of the terminal NH_2 group which gives a tentative octahedral geometry except in the case of Zn(II) and Mn(II) sulfadoxine complexes which are tetrahedral. The alteration successfully made to the structure and geometry of sulfadoxine is expected to modify its bioactivities and hence its virgin pharmaceutical potentials.

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