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DIVALENT METAL COMPLEXES OF 4-AMINO-N-PYRIMIDIN-2-YLBENZENE SULPHONAMIDE AND THEIR ANTIMALARIAL ACTIVITIES AGAINST *PLASMODIUM BERGHEI*

Adedibu C. Tella* and Joshua A. Obaleye

Department of Chemistry, University of Ilorin, Kwara State, Nigeria

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ABSTRACT. Coordination compounds of 4-amino-N-pyrimidin-2-ylbenzene sulphonamide (APS) were synthesized. The complexes were formulated as $[Co(APS)_2(H_2O)_2]$, $[Cu(APS)_2(H_2O)_2]$, $[Ni(APS)_2(H_2O)_2]$, $[Cd(APS)_2](H_2O)_2$, $[Fe(APS)_3](H_2O)_3$ and $[Mn(APS)_2(H_2O)_2]$ characterized by elemental analysis, conductivity, IR, UV-Vis, magnet moment and ^{1}H-NMR and mass spectroscopies. In all the complexes the metal ions coordinate through pyrimidinic nitrogen and sulphonamidic nitrogen of the two molecules of APS. The suggested structure for Cd(II) complex of APS is tetrahedral, while that of Cu(II), Mn(II) and Ni(II) APS complexes is octahedral. The inner coordination spheres were occupied by two water molecules in Co(II), Mn(II), Cu(II), Ni(II) APS complexes except Cd(II) with 2 molecules of water outside the coordination sphere. Fe(III) coordinates with 3 molecules of APS with 3 molecules of water outside the coordination sphere. The antiparasitic studies using *Plasmodium berghei* as test organism showed that the Fe(III) complex exhibits higher activity than chloroquine and ligand. All other complexes have lower antiparasitic activity.

KEY WORDS: Sulphonamide, Antimalarial activity, *Plasmodium berghei*

INTRODUCTION

The investigation of metal sulfonamide compounds has received much attention due to the fact that sulfonamides were the first effective chemotherapeutic agents to be employed for the prevention and cure of bacterial infections in humans [1]. All the sulphonamides are sulfur containing ligands. They are well known for their anticarcinogenic, antibacterial, antifungal, tuberculostatic and acaricidal activities [2]. It has been reported that biological activity of sulfur containing ligands get enhanced on coordination with metals [2]. The metal-chelates of sulphonamides have been found to be more bacteriostatic than the drugs themselves [3, 4]. The use of metal complexes as chemotherapeutic drugs has become a vibrant and growing area of research in recent time. Some of the metal based drugs already in market are cisplatin (anticancer drug), silverderma (silver complex of sulfadiazine for skin burn treatment) manufactured by Aldo union in Spain, flammazine (zinc complex of sulfadiazine for animal burn) manufactured by Durphar company, Spain and matrix metalloproteinase inhibitors (treatment of cancer) manufactured by British Biotech [5]. Despite major chemical successes and very encouraging results of biological screening of these anticancer and antimicrobial metals drugs complexes, little research has been conducted in development of antimalarial metal complexes, to deal with malarial parasites which had developed resistance against many existing antimalarial drugs. In continuation of our effort to find novel antimalarial drugs effective against chloroquine resistant strains malarial parasites [6-10], we have extended our study to include coordination compounds of 4-amino-N-pyrimidin-2-ylbenzene sulphonamide. The present account details the synthesis, characterization and antimalarial activities of 4-amino-N-pyrimidin-2-ylbenzene sulphonamide divalent metal complexes.

*Corresponding author. E-mail: ac_tella@yahoo.co.uk

EXPERIMENTAL

Materials and instrumentation

All the reagents and chemicals were used as obtained from Aldrich. The analyses of carbon, hydrogen and nitrogen were carried out on a Perkin-Elmer 204C microanalyser. IR spectra were obtained as KBr disc on a Perkin Elmer FTIR spectrophotometer. Metal analyses were carried out on Alpha 4 Atomic Absorption spectrophotometer. ^{1}H-NMR spectra were recorded with a Bruker AMX-200 Spectrometer in DMSO-d_6 (δ = 2.60 ppm). Chemical shifts for proton resonances are reported in ppm (δ) relative to tetramethylsilane. Mass spectra were recorded on a Micromass Platform spectrometer and Kratos concept IS Instrument using DMSO as solvent. UV-Vis spectra were obtained on Aquamate v4.60 spectrophotometer. Magnetic susceptibility of the complexes was determined at room temperature by the Gouy method [11]. Mercury tetrathiocynatocobaltate(II) $Hg[Co(NCS)_4]$ was used as calibrant.

General procedure of synthesis of metal complexes of APS

1 mmole of each of ($CoCl_2.6H_2O$, $NiCl_2.6H_2O$, $MnCl_2.4H_2O$, $CuCl_2.2H_2O$, $CdCl_2.2H_2O$ and $FeCl_3.6H_2O$) in 20 mL distilled water was added drop wise to a stirred alkaline solution 2 mmole (0.500 g) of APS in 60 mL of 0.1 M NaOH. The solution was stirred for 18 hours at room temperature as a pinkish, greenish, brownish, greyish, whitish and darkish brown formed for $[Co(APS)_2(H_2O)_2]$, $[Ni(APS)_2(H_2O)_2]$, $[Mn(APS)_2(H_2O)_2]$, $[Cu(APS)_2(H_2O)_2]$, $[Cd(APS_2](H_2O)_2$ and $[Fe(APS)_3](H_2O)_3$, respectively. Each precipitate was filtered and washed several times with distilled water and dried under vacuum.

$[Co(APS)_2(H_2O)_2]$. Pinkish solid, yield: 89%. M.wt = 592.93. M.p. > 300 ^{0}C. Anal. calcd. for $[C_{20}H_{22}N_8O_6S_2Co]$: C, 40.48; H, 3.71, N, 18.88; Co, 9.94. Found: C, 40.39; H, 3.82; N, 18.73; Co, 10.05. IR (KBr, cm^{-1}): 3446, 3300, 3247, 3152, 1594, 1417, 1275, 1142, 1111, 1089, 985, 837, 589, 553, 527. UV-Vis (DMSO): λ, nm: 411, 503, 562. ^{1}H-NMR (DMSO-d_6): δ 12.00 (OH), 6.11 (H_2N), 9.5 (H(4a)/H(6a).

$[Ni(APS)_2(H_2O)_2]$. Greenish solid, yield: 82%. M.wt = 592.70. M.p. > 300 ^{0}C. Anal. calcd. for $[C_{20}H_{22}N_8O_6S_2Ni]$: C, 40.49; H, 3.71; N, 18.90; Ni, 9.90. Found: C, 40.31; H, 3.60; N, 19.05; Ni, 9.82. IR (KBr, cm^{-1}): 3439, 1627, 1596, 1559, 1421, 1267, 1135, 990, 684, 586, 557. UV-Vis (DMSO): λ, nm: 400, 602, 752.

$[Mn(APS)_2(H_2O)_2]$. Brownish solid, yield: 75%. M.wt 588.94. M.p. > 320 ^{0}C. Anal. calcd. for $[C_{20}H_{22}N_8O_6S_2Mn]$: C, 40.75; H, 3.74; N, 19.02; Mn, 9.33. Found: C, 40.90; H, 3.70; N, 18.84; Mn, 9.18. IR (KBr, cm^{-1}) 3423, 3355, 3258, 1652, 1593, 1326, 1262, 1155, 942, 640, 523. UV-Vis (DMSO) λ, nm: 380. MS (positive Cl-methane): m/z, (relative intensity): 96 (100), 126 (90), 156 (80), 185 (100), 215 (16), 233 (40), 279 (30), 289 (2), 406 (6).

$[Cu(APS)_2(H_2O)_2]$. Greyish solid, **y**ield: 72%. M.p. > 300 ^{0}C. M.wt = 597.55. Anal. calcd. for $[C_{20}H_{22}N_8O_6S_2Cu]$: C, 40.16; H, 3.68; N, 18.74; Cu, 10.63. Found: C, 39.88; H, 3.75; N, 18.66; Cu, 10.78. IR (KBr, cm^1): 3446, 3300, 1633, 1593, 1556, 1454, 1422, 1278, 1128, 1081, 972, 556. UV-Vis (DMSO): λ, nm: 865.

$[Cd\ (APS_2](H_2O)_2$. Whitish solid, yield: 68%. M.p. > 330 ^{0}C. M.wt = 753. Anal. calcd. for $[C_{20}H_{22}N_8O_6S_2Cd]$: C, 37.13; H, 3.40; N, 17.33; Cd, 17.39. Found: C, 37.20; H, 3.38; N, 17.50;

Cd, 17.48. IR (KBr, cm^{-1}): 3454, 3316, 3244, 3152, 1596, 1582, 1500, 1412, 1274, 1141, 1007, 980, 845, 588, 554, 451. UV-Vis (DMSO) λ, nm: 256, 285.

$[Fe(APS)_3](H_2O)_3$. Darkish brown solid, yield: 72%. M.p. > 350 ^{0}C, M.wt = 856.85, Anal. calcd. for $C_{30}H_{33}N_{12}O_9S_3Fe$; C, 42.01 H, 3.85; N, 16.81; Fe, 6.52. Found: C, 42.25; H, 3.68; N, 16.78; Fe, 6.50. IR (KBr, cm^{-1}): 3424, 3356, 3261, 2938, 1652, 1594, 1493, 1326, 1263, 1107, 1157, 1094, 945, 550. UV-Vis (DMSO) λ, nm: 375, 400.

Antiparasitic screening

Plasmodium berghei and mice were collected from IMRAT, University of Ibadan, Ibadan Nigeria. Mice for the experiment were infected as described by previous worker [12]. Eighty Swiss mice (male) were divided into groups of nine animals each and kept in cages fed with mice cubes and water ad *libitum*. Group 1: control, group 2: chloroquine, group 3: 4-amino-N-pyrimidin-2-ylbenzene sulphonamide (APS), group 4: $[Co(APS)_2(H_2O)_2]$, group 5: $[Ni(APS)_2(H_2O)_2]$, group 6: $[Mn(APS)_2(H_2O)_2]$, group 7: $[Cu(APS)_2(H_2O)_2]$, group 8: $[Cd(APS)_2](H_2O)_2$ and group 9: $[Fe(APS)_3](H_2O)_3$.

The mice in each group were marked for easy identification. The mice received 0.2 mL of 1 x 10^6 parasitized erythrocytes suspended in buffered physiological saline (pH 7.4) inoculated intravenously. The mice were left for 4 days; their levels of parasitaemias were monitored daily by counting parasites in blood smear, fixed with 70% methanol and giemsa stained. The slide were then rinsed and allowed to dry. The slides were viewed under the microscope with magnification of 100. The level of parasitaemia was then determined by counting the number of infected erythrocytes/1000 erythrocyctes on tail blood smears stained with giemsa. 1 μg/mL solution of each of the ligands and complexes was prepared. 0.4 mL of each of the solution prepared with dimethylsulphoxide was injected daily into the mice in each group from day 0 to day 3 of infection. Levels of parasitaemia were determined on day 4. Only physiological saline solution was given to the control animals. The results were expressed as the percentage of infected cells or inhibition of parasitaemia calculated from the equation.

$$\% \text{ inhibition} = 100 - \frac{\text{Estimated no of infected parasitaemia treated with compounds}}{\text{Estimated no of infected parasitaemia treated with no compounds}}$$

RESULTS AND DISCUSSION

The metal complexes of 4-amino-N-pyrimidin-2-ylbenzene sulphonamide are generally soluble in DMSO except $[Mn(APS)_2(H_2O)_2]$ and $[Cd(APS)_2](H_2O)_2$ which are sparingly soluble. All the complexes are insoluble in organic solvents. The metal halide salts react with the 4-amino-N-pyrimidin-2-ylbenzene sulphonamide according to the general equation.

$$Mx_2.nH_2O + 2APS \rightarrow M(APS)_2(H_2O)_2$$

The elemental analysis of the complexes revealed that the compounds have a metal:ligand stoichiometry of 1:2, corresponding to a general formulae: $[M(APS)_2.nH_2O]$ (where M = Mn(II), Co(II), Ni(II), Cd(II) and Cu(II) and APS = amino-N-pyrimidin-2-ylbenzene sulphonamide). The analytical data are in good agreement with the proposed stoichiometry of the complexes.

All the complexes were of non-electrolytes type, as the measured conductivities were in the range 7.2-10.3 $\Omega^{-1}cm^2\ mol^{-1}$ [13].

The complexes were characterised by elemental analysis, UV-VIS and IR. The $[Co(APS)_2(H_2O)_2]$ were analysed by ^{1}H-NMR while $[Mn(APS)_2(H_2O)_2]$ was also characterized

by mass spectrometry. From spectroscopic studies and analytical data, suggested structures of the complexes are shown in Figures 1, 2 and 3.

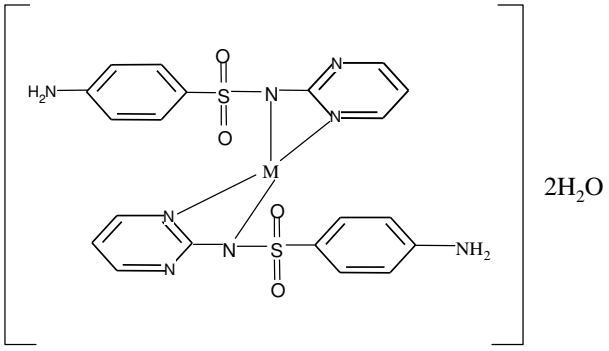
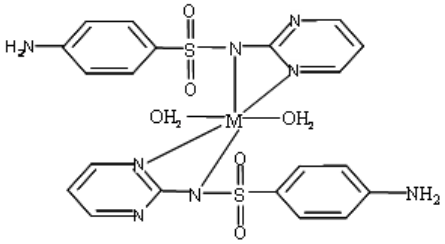


Figure 1. Proposed structure for Cd(II) APS complexes.



M = Co(II), Cu (II), Mn(II) or Ni(II)

Figure 2. Proposed structure for APS metal complexes.

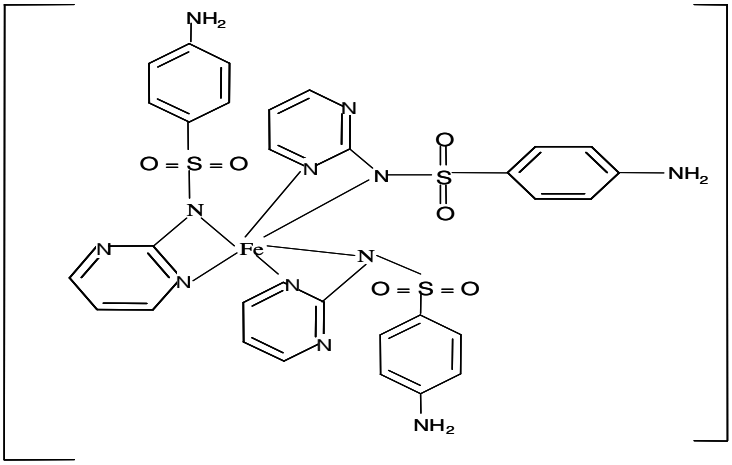


Figure 3. Proposed structure for Fe(III)APS complex.

FT-IR spectra

The assignments of infrared spectra of APS and its complexes are given in Table 1. The infrared spectrum of the complexes was recorded down to the far IR region of 400 cm^{-1} and compared with that of APS ligand. The bands near 3460 and 3290 cm^{-1} assigned to ν_{asy} and ν_{sy} (N-H) vibrations of the NH_2 group are not significantly shifted with respect to those of the free ligand (3424 and 3315 cm^{-1}). The slight modification may be as a result of increased acidity of the NH_2 group derives mainly from polarization effect which arises in the complex, rather than from direct coordination to the metal ion. It could even be due to hydrogen bonds involving the amino groups. This is an indication that the NH_2 group in the free ligand is not affected by coordination to the metal ion [14]. The presence of coordinated water molecules in all the complexes has been inferred on the basis of two bands around 3450-3300 cm^{-1} which overlap with νNH_2 on the pyrimidine ring [15] and appearance of a vibrational band at 630-750 cm^{-1} ($\nu M\text{-}OH_2$).

Table 1. Selected IR data (cm^{-1}) of APS and its complexes (νNH_2 sym or asy/νH_2O).

Complexes/ligand	νNH_2 sym/asym /νH_2O	$\nu C{=}N/\delta NH_2$	νSO_2 (asy)	νSO_2 (sym)	$\nu S–N$	$\nu M–N$
APS	3424 s, 3356 s	1653m	13.25 s	1156 s	942 vs	–
$[Cd(APS)_2](H_2O)_2$	3454 m,b, 3316 s	1596 s	1274 m	1141 m	980 s	554 s
$[Co(APS)_2(H_2O)_2]$	3446 m,b	1594 s	1275 s	1142 s	985 m	553 s
$[Mn(APS)_2(H_2O)_2]$	3423 s, 3355 s	1593 s	1262 m	1155 vs	942 s	523 vs
$[Ni(APS)_2(H_2O)_2]$	3439 s,b	1627 m	1267 s	1135 s	990 m	557 m
$[Cu(APS)_2(H_2O)_2]$	3446 s,b, 3300 s,b	1633 m	1278 s	1128 s	972 m	556 s
$[Fe(APS)_3](H_2O)_3$	3424 s, 3356 s	1652 s	1263 m	1157 vs	945 s	550 s

s = strong, m = medium, vs = very strong, b = broad.

The strong band related to the symmetrical and asymmetrical stretching of the $\nu(SO_2 – NH)$ moiety at 1325 and 1156 cm^{-1}, in the sulphadiazine show important change upon complexation. The first shifted to lower wavenumber by about (33-67 cm^{-1}) and the second shifted also to lower wavenumber (by about 10-20 cm^{-1}). Those changes suggest coordination of the metal ion to the nitrogen of the (SO_2-NH) moiety. The band at 942 cm^{-1} corresponding to ν(S-N) shifted to higher frequency (~ 990 cm^{-1}) upon complexation, this further substantiates the coordination of metal ion via sulfamito nitrogen atom of the APS [16].

The band at 1653 cm^{-1} attributed to $\nu C{=}N$ of pyrimidine was also shifted to lower wavenumber by about 20 cm^{-1} in the complex. This fact is in agreement with the interaction through the pyrimidine nitrogen atom [17]. The appearance of new bands around 550-558 cm^{-1} in the complexes have been assigned to νM-N.

Electronic spectra of APS and its complexes

The electronic spectra of APS and its complexes are shown Table 2. The electronic spectrum in DMSO of APS gave absorption band at (35211 cm^{-1}) 284 nm, the band is assigned to $\pi\rightarrow\pi^*$. The cadmium ion has its 5d orbital completely vacant and hence ligand to metal (L→M) binding can take place by the acceptance of a one pair of electron from the donor nitrogen atom of the ligand. The same band is observed at $[Cd(APS)_2](H_2O)_2$, as expected no extra bands were observed for this complex, with ^1S spectroscopic term, respectively whereas extra bands have been observed for (Ni(II), Co(II), Fe(III) and Cu(II) complexes, which have been attributed to d-d transition. The Mn(II) complex show two bands at (26316 cm^{-1}) 380 nm assigned to $\pi\rightarrow\pi^*$

and (22523 cm^{-1}) 444 nm attributed to metal ligand charge. No d-d transition is expected for Cd(II) complex.

Table 2. Electronic spectra of APS and its complexes.

Complexes/ligand	Wavelength (nm)	Energies (cm^{-1})	Assignment
APS	284	35211	$\pi \rightarrow \pi^*$ /n$\rightarrow\pi^*$overlap
$[Co(APS)_2(H_2O)_2]$	411	24331	$^4T_{1g} \rightarrow {}^4T_{1g}(P)$
	503	19881	$^4T_{1g} \rightarrow {}^4A_{2g}$
	562	17794	$^4T_{1g} \rightarrow {}^4T_{2g}$
$[Ni(APS)_2(H_2O)_2]$	400	25000	$^3A_{2g} \rightarrow {}^3T_{1g}(P)$
	602	16611	$^3A_{2g} \rightarrow {}^3T_{1g}$
	752	13298	$^3A_{2g} \rightarrow {}^3T_{2g}$
$[Mn(APS)_2(H_2O)_2]$	380	26316	$n\rightarrow\pi^*$
	444	22523	MLCT
$[Cu(APS)_2(H_2O)_2]$	865	11561	$^2E_g \rightarrow {}^2T_{2g}$
$[Cd(APS)_2](H_2O)_2$	274	36496	$\pi \rightarrow \pi^*$
$[Fe(APS)_3](H_2O)_3$	375	26667	$n\rightarrow\pi^*$
	400	25000	MLCT

The electronic configuration of $[Fe(APS)_3](H_2O)_3$ is d^5. Metal ligand charge transfer and $n\rightarrow\pi^*$ occur at (26667 cm^{-1}) 375 nm, (25000 cm^{-1}) 400 nm. The electronic configuration of $[Co(APS)_2(H_2O)_2]$ is d^7 with spectroscopic ground term ^4F. The complex showed three bands in the visible region. The absorption band at (24331 cm^{-1}) 411 nm) may be assigned to $^4T_{1g} \rightarrow {}^4T_{1g}(P)$, the second band (19881 cm^{-1}) 503 nm is assigned to $^4T_{1g} \rightarrow {}^4A_{2g}$ and third band (17794 cm^{-1}) 562 nm is attributed to $^4T_{1g} \rightarrow {}^4T_{2g}$. The electronic configuration of $[Ni(APS)_2(H_2O)_2]$ is d^8 and a spectroscopic ground term is ^3F. The absorption band at (25000 cm^{-1}) 400 nm is assigned to $^3A_{2g} \rightarrow {}^3T_{1g}(P)$, a second band at (16611 cm^{-1}) 602 nm is assigned to $^3A_{2g} \rightarrow {}^3T_{1g}$ and the third band centered at about (13298 cm^{-1}) 752 nm is assigned to $^3A_{2g} \rightarrow {}^3T_{2g}$. The assignments are in conformity with the proposed octahedral geometry for the complex [18]. As expected, Cu(II) complex showed a broad band at (11561 cm^{-1}) 865 nm attributed to $^2E_g \rightarrow {}^2T_{2g}$.

Magnetic susceptibility

Magnetic moments of each of the complexes are given in Table 3. Examination of these data reveals that magnet moment of 0.4 B.M. for Cd(II) complex confirms that the complex is essentially diamagnetic. The magnetic moment μ_{eff} for the complexes of Fe^{3+} (d^5) and Mn^{2+} (d^5) were found to be 5.34 B.M. and 5.56 B.M., respectively. These values indicate that the complexes are high spin type paragmagnetic. It lies within the octahedral range [19]. Ni^{2+} (d^8) and Co^{2+} (d^7) complexes have shown magnetic moment value 3.78 B.M. and 4.54 B.M, these values suggest octahedral geometry which is in good agreement with data of electronic transition [20]. Finally, the μ_{eff} of the Cu^{2+} (d^9) complexes was found to be 1.86 B.M. which lies within the expected value for one electron.

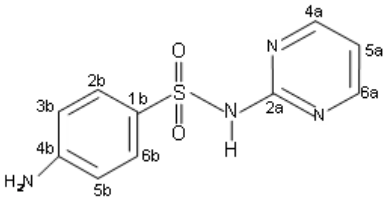
Table 3. Magnetic susceptibility and conductivity measurement of APS metal complexes.

Complexes	Magnetic moment μ (B.M.)	Conductivity Ohm^{-1} cm^2 mol^{-1}
$[Co(APS)(H_2O)_2]$	4.67	7.4
$[Cu(APS)_2(H_2O)_2]$	1.86	9.4
$[Ni(APS)_2(H_2O)_2]$	3.78	8.6
$[Mn(APS)_2(H_2O)_2]$	4.45	7.8
$[Cd(APS)_2](H_2O)_2$	0.4	8.8
$Fe(APS)_3](H_2O)_3$	5.34	10.3

Proton NMR spectra of APS and $[Co(APS)_2(H_2O)_2]$

The assignment of proton NMR spectra of APS and $[Co(APS)_2(H_2Os)_2]$ are made by comparison with the spectra of APS as shown in Table 4. The assignment of the signals have been carried out with respect to previous studies of Co(II) streptonigrin complex [21]. A comparison of the data for Co(II) complex with respective sulfadiazine ligand shows that the (SO_2-NH) proton at 11.3 ppm completely disappeared in the spectrum of the $[Co(APS)_2(H_2O)_2]$ indicating that NH proton was removed by chelation with Co(II). This observation in conjunction with the infrared spectra studies for the compounds corroborates with deprotonation of NH proton and subsequent coordination of the sulfonamidic nitrogen to the metal ion. The peak at δ = 6.11 ppm in the ligand characteristic of proton of NH_2 remains almost unaffected in complex indicating that the NH_2 group is not involved in coordination. Moreover, the downfield shift for H (4a)/H(6a) resonance (8.5 to 9.5 ppm) could be related to the proximity of the Co(II) which can be explained by a direct interaction, as in solid state, between Co(II) and pyrimidinic nitrogen. New peak at 12.00 ppm due to proton of OH appeared in the complex, indicates probable coordination of H_2O to the metal ion.

Table 4. ^{1}H-NMR spectra of APS and Co(II)APS complex.



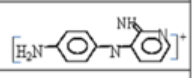
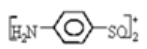
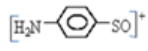
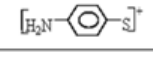
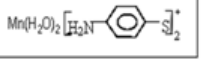
Assignment	^{1}H-NMR of APS (δ)	^{1}H-NMR of $[Co(APS)_2(H_2O)_2]$ (δ)
OH	-	12.00
H_2N	6.11	6.11
H(2a)H	11.3	-
H(4a)/H(6a)	8.5	9.5

Mass spectroscopy of $[Mn(APS)_2(H_2O)_2]$

The mass spectra, relevant m/z ratios and tentative assignments of $[Mn(APS)_2(H_2O)_2]$ are shown in Table 5. The peak observed at m/z 406 corresponds to $Mn(H_2O)_2[C_{12}H_{12}S_2O_2]^+$ indicating pyrimidine has been lost from the complex. The peak at m/z 251 is due to the 4-amino-N-pyrimidin-2-ylbenzene sulphonamide $C_{10}H_9N_4O_2S$. Intense band was observed at m/z 185

attributed to loss of SO_2. Other peaks are m/z 140 $[C_6H_6NSO]^+$ attributed to loss of oxygen from m/z 156.

Table 5. Mass spectra assignment for $[Mn(APS)_2(H_2O)_2]$.

M/z	Relative intensity (%)	Assignment
251	85	M.H$^+$
185	100	
156	79	
140	54	
126	89	
406	50	

The melting points and colour of the complexes are quite distinct from that of the corresponding ligands which is an evidence of formation of the complex.

Based on the above spectroscopic studies in conjunction with analytical data, the proposed structure for Cd(II) complex of APS is tetrahedral, while that of Cu(II), Mn(II) and Ni(II) APS complexes are octahedral. In all the complexes the metal ions coordinate through pyrimidinic nitrogen and sulphonamidic nitrogen of the two molecules of APS. The inner coordination spheres were occupied by two water molecules in Co(II), Mn(II), Cu(II), Ni(II) APS complexes except Cd(II) with 2 molecules of water outside the coordination sphere. Fe(III) coordinates with 3 molecules of APS with 3 molecules of water outside the coordination sphere. The proposed structures are shown in Figures 1, 2 and 3.

Antiparasitic screening

The results % reduction in parasitaemia of the ligand and chloroquine are presented in Table 6 and the complexes in Table 7. The complexes were screened for their potencies against a causative organism of malarial diseases. The antipasmodial activity was evaluated using mice infected with *Plasmodium berghei*. All the complexes showed relatively lower antimalarial activity against the tested parasite than chloroquine and ligand except Fe(III) complex. Five of the metal complexes showed lower antiplasmodial activity with % reduction in parasitaemia ranging from 37-47%. The sixth complex Fe(III) complex % reduction in parasitaemia is 74%.

Table 6. Percentage reduction in parasitaemia of ligand and chloroquine.

	No	Average % parasitaemia in mice before application	Average % parasitaemia after application	Percentage reduction in parasitaemia
Chloroquine	C	40	15	63
APS	D	60	28	53

Table 7. Percentage parasitaemia of metal complexes.

	No	% Average parasitaemia before administration	% Average parasitaemia after administration	% Reduction in parasitaemia
$[Cd(APS)_2](H_2O)_2$	1	34	19	44
$[Cu(APS)_2(H_2O)_2]$	2	26	16	38
$[Ni(APS)_2(H_2O)_2]$	3	34	22	35
$[Mn(APS)_2(H_2O)_2]$	4	26	17	35
$[Fe[(APS)_3](H_2O)_3]$	5	38	10	74
$[Co(APS)_2(H_2O)_2]$	6	36	19	47

Coordination of Ni(II), Co(II), Mn(II), Cd(II), Cu(II) to 4-amino-N-pyrimidin-2-ylbenzene sulphonamide whereas coordination to the iron enhances antiplasmodia activity of the drugs. This could be due to the complexes binding first without being decomposed at the receptor site and also the deposition of free metal ions in the membrane of the parasites. The parasite needs iron for their development thereby making them to look for bait which will lead consequently to death by the poison (APS). The same reason account for the high activity of iron complexes of the drugs as compared to other metal ion complexes. This finding is in agreement with the results of studies carried out by Biot *et al*. [22]. The release of the drug into the target site made the availability of the free metal ion, e.g. Fe^{3+} which is very essential to the body system. Iron is important in the human body because of the occurrence in many heamoproteins such as haemoglobin, myoglobin and cytochromes. Also, the metal ions could be reduced to its free state and could be toxic to the membrane of plasmodium in which man could guard its content zealously for a better living.

CONCLUSIONS

Divalent metal complexes of 4-amino-N-pyrimidin-2-ylbenzene sulphonamide are reported. The complexes were characterized by elemental analysis, magnetic susceptibility, electronic, IR, ^{1}H-NMR and mass spectroscopies. All the complexes are found to have octahedral geometry except Cd(II) which is tetrahedral. The antiparasitic studies using *Plasmodium berghei* as test organism showed that the Fe(III) complex exhibits higher activity than chloroquine and ligand. All other complexes have lower antiparasitic activity.

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