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Antimalarial and Antimicrobial Activities of some Heteroleptic Metal(II) Complexes of Sulfadiazine–Vitamin C: Synthesis and Spectroscopic Studies

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Abstract

Some new Ni(II), Zn(II), Co(II), Cu(II), and Cd(II) of mixed Sulphadiazine and Vitamin C complexes have been synthesized and characterized by different spectroscopic techniques such as FT-IR, elemental analysis, molar conductivity, and magnetic measurements. Both ligands used for this research work act as bidentate ligands towards the central metal ions coordinating through the nitrogen atoms of >C=N–, NH_2 groups of Sulphadiazine and oxygen atoms of OH, CO groups of Vitamin C. Tetrahedral and square-planar geometries have been proposed for the complexes. The complexes are stable under atmospheric conditions. The ligands and their complexes were screened for antimicrobial activities against some isolated organisms: *Klebsiella pneumoniae, Bacillus subtilis, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa* and *Enterococcus faecalis* to evaluate their microbial inhibiting potential. The derived complexes were found to exhibit an increased inhibitory action against the organisms when compared to the free ligands. The percentage reduction in *parasitaemia* for the compounds was also evaluated against *Plasmodium berghei*. In this realm, $[Cd(Su)(Vit)]Cl_2$ showed the highest activity (89%) as compared to other compounds: Sulphadiazine, Ni(II), Zn(II), Co(II), and Cu(II) complexes are 70, 50, 81, 76, and 77%, respectively, Vitamin C showed no activity.

Keywords: Sulfadiazine, Antimalarial, Vitamin C, Physicochemical, Metal-drug complexes, Antimicrobial.

Introduction

Antimicrobial Resistance (AMR) among different infectious agents is well known worldwide as a health threat, thereby increasing the world's mortality rate, resulting in about 17 million deaths globally per year in children and the elderly (Gülcan et al. 2012, Bamigboye et al. 2021a, 2021b). Increasingly, governments around the world are beginning to pay attention to problems associated with infectious diseases, as it presents some serious threat towards achieving modern medicine. Metal complexes are the focus of drug designs due

to the success of metallodrugs like auranofin and cisplatin (Ejidike and Ajibade 2015, Palermo et al. 2021). This has expanded the database on chemotherapeutic agents which are less toxic with improved anticancer, antioxidant, and antimicrobial activities. Thus, metal complexes serve as lead compounds for the replacement of existing chemotherapeutic agents in the combat against toxicity and resistance (Ejidike et al. 2019, Bamigboye et al. 2020, Ejidike et al. 2021).

A sulphonamide is any member of the class which contains the group —SO_2N. This class includes several groups of drugs used in the treatment of bacterial infections, diabetes mellitus, hypertension, and gout (Mounika et al. 2010). Sulfadiazine is a sulfonamide with well-known antibacterial activities. The effectiveness of the sulpha drugs helps upon coordination with a metal salt (Lachapelle and Drouin 2011). From research, it has been observed that sulfadiazine complexes have gained considerable importance as a result of biological activity. The sulfonamides were first recognized as effective agents to be employed systematically.

Ascorbic acid is one form of Vitamin C, which can be synthesized industrially from glucose. It is a reducing agent and antioxidant. It reacts with oxidants of the reactive oxygen species, such as the hydroxyl radical that is capable of causing damage to animals and plants at the molecular level due to their relationship with nucleic acids, proteins, and lipids (Ikokoh et al. 2015, Bharathi et al. 2015). Owing to the increased resistance to different sulpha drugs by microorganisms, many efforts have been put towards developing new therapeutic agents. Hence, the need to synthesize a new resistant drug that can control many infectious diseases or activities (Ikokoh et al. 2015, Koleva et al. 2021). In this regard, the synthesis of metal complexes have received great attention (Bharathi et al. 2015, Ejidike and Ajibade 2015, Dikio et al. 2017, Bamigboye et al. 2020).

In continuation of our efforts towards the development of metal-based chemotherapeutic agents, the present study deals with the synthesis and characterization of mixed sulfadiazine-vitamin C metal(II) complexes, their antimalarial and antibacterial potentials.

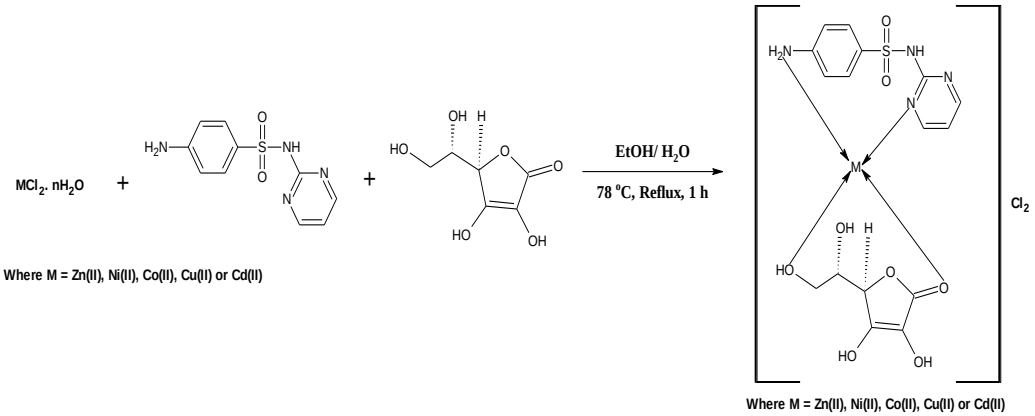
Materials and Methods

Chemicals and apparatus

All chemicals and reagents were of good analytical grade without further purification. Sulphadiazine and Vitamin C were collected from Rajrab Pharmaceutical Company, Ilorin, Nigeria. The chloride of the metal salts and other chemicals were obtained from Sigma-Aldrich (Johannesburg, South Africa). The molar conductivity was determined on the HANNA instrument conductivity meter with a cell constant of 0.73. The elemental analyses (CHN) of the complexes were recorded on a Perkin–Elmer 204C micro analyzer at Medac Limited Company, Brunnel Science Centre (Eghan, United Kingdom). The melting point of the ligands and their complexes were recorded on the Gallenkamp apparatus. Chloroquine sensitive *Plasmodium berghei* (NK 65 strain) was received from the Nigeria Institute of Medical Research. The FT-IR spectra of the free ligands and the synthesized complexes were recorded on FT-IR spectrophotometer, Perkin Elmer System (Spectrum 2000) in the range of 4000–400 cm^{-1}.

Synthesis of complexes

The complexes were prepared in line with the method reported in the literature by Lawal and Obaleye (2007) and Bamigboye et al. (2021a) with slight modifications. Hot ethanol (20 ml) solution of Sulphadiazine (1 mmol, 0.25 g) was added to a cold solution of Vitamin C (1 mmol, 0.18 g) in 10 ml of distilled water. The solution of each metal salt (1 mmol) was also dissolved in 10 ml of distilled water. The prepared solutions were thoroughly mixed and stirred for 60 min. at 78 °C, and then concentrated to half of the original volume. It was allowed to cool and left to stand in a refrigerator for 24 h. The coloured precipitate formed was isolated by filtration under a vacuum. It was washed with mixed cold ethanol water and dried in a desiccator over silica gel (Scheme 1).



Scheme 1: Synthetic pathway and chemical structures of the metal(II) complexes of Sulfadiazine-Vitamin.

Antibacterial activities

With little modification, the procedure reported by Ahmed et al. (2017) and Bamigboye et al. (2021b) was adopted for this study. Nutrient agar (7 g) was measured into a round bottom flask containing 250 ml of distilled water. This was homogenized and sterilized in an autoclave at 121 ± 1 °C for 15 min. The molten agar was introduced into sterile Petri-dishes and allowed to set. Holes were bored into each plate using sterile cork borer (6 mm) standardized inoculum of each test organism (*Klebsiella pneumoniae, Bacillus substilis, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa,* and *Enterococcus faecalis*) were introduced onto the agar plates using a sterile swab stick. The saturated solutions were then filled into each borehole using a sterilized pipette. This was allowed to stay on the workbench for 30 min. and then incubated in an upright position at 37 ± 1 °C for 24 h. The clear zones of inhibitions were measured to determine the antibacterial activity of the synthesized complexes against the tested organisms.

Antimalarial activities

Malaria parasite

With little modification, the procedure reported by Tella and Obaleye (2010) was adopted for this assay. The chloroquine-sensitive *Plasmodium berghei* (NK 65 strain) was obtained from the Nigeria Institute of Medical Research. The parasites were maintained weekly by blood passage in mice.

Inoculation of experimental mice

The mice were infected intraperitoneally with standard inoculum (0.2 ml of 1 x 10^7 parasitized red blood cells-RBCs). The inoculum was from a single donor mouse previously infected with *P. berghei* (33 % parasitaemia).

Estimation of percentage parasitaemia

Percentage *parasitaemia* was evaluated at the end of the observed period of 28 days with the use of the following formula:

$$\% \text{ Parasitaemia} = \frac{Parasitized\ RBC}{Parasitized\ RBC\ +\ Non\ parasitized\ RBC} \times 100$$

Animal grouping and extract administration

The animals were randomly divided into 6 groups of 5 mice each after confirmation of *parasitaemia*, 72 h post-inoculation. Groups 1–4 were administered orally with test agents in varied concentrations for 5 days. Group 5 received the standard drug for 5 days, while group 6 control was left untreated but was administered using the same volume of distilled water.

Physicochemical characteristics

Aqueous solubility

Saturated solution (15 ml) of the ligands and their complexes were prepared at a determined temperature. It was allowed to evaporate to dryness using an evaporating dish. The mass of the residues was weighed and reported. The aqueous solubility was calculated using the following equation (Onwudiwe and Ajibade 2012):

$$S = \frac{\text{Mass}}{\text{Volume}} \times 100$$

Thermal and acid stability

The solution of the test compounds (0.15 mg/ml) was diluted. Five different portions of 0.15 mg/ml of the solution of the compounds were introduced. The temperatures were adjusted to 15 °C, 20 °C, 25 °C, and 30 °C. They were left to stand for about 24 hours and the absorbance was collected and recorded. The concentration of the solutions was prepared within the pH of 1 to 5. A similar thermal procedure was followed to determine the acid stability (Onwudiwe and Ajibade 2012).

Results and Discussion

Chemistry of the synthesized compounds

The physicochemical and analytical data of the test compounds presented in Table 1 is of the formula type: $[M(L–L)]X_2$ (where M = Ni(II), Zn(II), Co(II), Cu(II), and Cd(II); L–L = Sulfadiazine–Vitamin C; X = Cl). The metal complexes were obtained by the reaction of metal salts and Sulfadiazine–Vitamin C ligands have been synthesized in a 1:1:1 mole ratio as shown in Scheme 1. The elemental analysis of the complexes was found to be in good agreement between the experimental and the calculated values (Table 1). They are stable at room temperature and in powdery form and exhibited a melting point of less than 300 ºC (Ejidike and Ajibade 2017, Bamigboye et al. 2021a, 2021b). The synthesized complexes were obtained in good quantitative yield ranging from 50 to 75% for nickel complex ($C_{16}H_{18}N_4O_8SCl_2Ni$, 556.00 g/mol) to zinc complex ($C_{16}H_{18}N_4O_8SCl_2Zn$, 562.72 g/mol).

Molar conductivity and magnetic moment measurements

The molar conductivity data as provided in Table 1, showed that $[Ni(Su)(Vit)]Cl_2$, $[Zn(Su)(Vit)]Cl_2$, $[Co(Su)(Vit)]Cl_2$, $[Cu(Su)(Vit)]Cl_2$, and $[Cd(Su)(Vit)]Cl_2$ complexes were found to be 88, 73, 94, 79, and 72 $\Omega^{-1}cm^2mol^{-1}$**,** respectively, indicating that all the synthesized metal complexes are 1:1 electrolyte in nature (Ejidike and Ajibade 2017, Bamigboye et al. 2021a, 2021b). The magnetic moment for the complexes at room temperature is within the range of 2.00 to 5.00 B.M, indicating that they are diamagnetic and paramagnetic in nature. This is an indication of distorted tetrahedral geometries for the metal compounds environment with MLCT except for nickel and copper complexes in square planner geometry following previous reports (Aiyelabola et al. 2012, Ejidike and Ajibade 2017, Ejidike et al. 2021).

IR spectral studies

The IR spectra of the ligands and their complexes are presented in Table 2. The band at 3400 cm^{-1} in Sulphadiazine is due to $\nu(NH_2)$. It was shifted to higher frequencies indicating the coordination of nitrogen present in the amine group to the central metal ions. The presence of $\nu(SO_2)$ group in Sulphadiazine exhibited two bands at 1339 cm^{-1} and 1160 cm^{-1} characteristic of asymmetric and symmetric stretching vibration, respectively. No significant shift was observed in the complexes suggesting that $\nu(SO_2)$ group did not participate in the coordination (Ajibade et al. 2006, Tella and Obaleye 2010). The spectrum of Vitamin C indicates a frequency band at 1717 cm^{-1} which are shifted to high frequencies in the range 1730–1743 cm^{-1} in the spectra of the complexes as attributed to carbonyl group participation. This also indicates that coordination occurs through the oxygen of the carbonyl group (Pouralimardan et al. 2017, Ejidike et al. 2021).

In the same manner, ν(O–H) stretching vibration in the Vitamin C ligand spectrum appeared at 3370 cm^{-1}. However, this banc was shifted with the range 334–3425 cm^{-1} in

the spectra of the metal complexes, suggesting the involvement of the hydroxyl group in the coordination sphere (Ejidike and Ajibade 2015, Dikio et al. 2017, Bamigboye et al. 2020). The band observed at 1649 cm^{-1} in Sulfadiazine is due to –C=N– stretching vibration which undergoes a hypsochromic shift in the range 1657 – 1675 cm^{-1} (Ajibade et al. 2006). This is an indication of the bonding of azomethine nitrogen ν(>C=N–) group of the ligand to the central metal ion (Ajibade et al. 2006, Ejidike and Ajibade 2017). New weak nonligand bands that are not found in the Sulphadiazine and Vitamin C ligands appeared in the ranges 553–572 cm^{-1} and 436–475 cm^{-1} in the complexes spectra attributable to ν(M-N) and ν(M-O) vibrations, respectively (Ejidike and Ajibade 2016, 2017, Pouralimardan et al. 2017, Bamigboye et al. 2021a, 2021b).

Antimalarial activities

The percentage reduction in *parasitaemia* for Sulphadiazine, $[Ni(Su)(Vit)]Cl_2$, $[Zn(Su)(Vit)]Cl_2$, $[Co(Su)(Vit)]Cl_2$, $[Cu(Su)(Vit)]Cl_2$, and $[Cd(Su)(Vit)]Cl_2$ complexes are 70, 50, 81, 76, 77, and 89 respectively, while Vitamin C showed no activity. Based on the data shown in Table 3 and Figure 1, it can be seen that the complexes demonstrated higher activities than their parent ligands. However, $[Ni(Su)(Vit)]Cl_2$ showed the least activity as compared to other complexes against the *Plasmodium berghei*. Coordination of the free ligands to the central metal ions helps to increase the activity of the complexes as potential chemotherapeutic agents. It also indicates that coordination of the metal ion to the ligands enhanced their antimalarial activities. This result was found to be in good agreement with the result of the study which was reported by Biot et al. (2011).

The central metal ion can be decreased to its free state and be harmful to the membrane of the *Plasmodium*. It is therefore, evident that all the tested complexes displayed moderate to high growth inhibitory activity, in particular compounds $[Cd(Su)(Vit)]Cl_2$, $[Zn(Su)(Vit)]Cl_2$, $[Cu(Su)(Vit)]Cl_2$, $[Co(Su)(Vit)]Cl_2$ (ranged from 76–89%), respectively. $[Cd(Su)(Vit)]Cl_2$ complex exhibited the highest toxicity against *Plasmodium berghei* than other complexes (Figure 1). The wide distribution in tissues and production of degenerative alterations in organs may be responsible for the higher toxicity of Cd(II) ions (Wan and Zhang 2012). The antimalarial activity orders of the metal(II) complexes of Sulphadiazine–Vitamin C can be arranged as follows: $[Cd(Su)(Vit)]Cl_2$ > $[Zn(Su)(Vit)]Cl_2$ > $[Cu(Su)(Vit)]Cl_2$ > $[Co(Su)(Vit)]Cl_2$ > $[Ni(Su)(Vit)]Cl_2$ > [Sulphadiazine].

Table 1: Physico-chemical and analytical data of the ligands and the metal(II) complexes

Ligands/ Complexes	Empirical Formula	F.Wt. (g) (%)	Yield	Colour	Melting point (°C)	Elemental analysis (%) Calcd. (Found)			Conductivity $\Omega^{-1}cm^2mol^{-1}$	μeff B.M.
						C	H	N		
Sulphadiazine [Su]	$C_{10}H_{10}N_4O_2S$	250.28	–	White	252–253	–	–	–	–	–
Vitamin C [Vit]	$C_6H_8O_6$	176.12	–	White	190–192	–	–	–	–	–
$[Ni(Su)(Vit)]Cl_2$	$C_{16}H_{18}N_4O_8SCl_2Ni$	556.00	50	Green	268–269	34.56 (35.40)	3.26 (3.36)	10.08 (9.23)	88	2.96
$[Zn(Su)(Vit)]Cl_2$	$C_{16}H_{18}N_4O_8SCl_2Zn$	562.72	75	Cream	271–273	35.34 (34.98)	3.66 (3.31)	9.70 (9.32)	73	–
$[Co(Su)(Vit)]Cl_2$	$C_{16}H_{18}N_4O_8SCl_2Co$	556.24	60	Grey	260–261	35.74 (35.45)	3.71 (3.38)	9.81 (10.13)	94	4.00
$[Cu(Su)(Vit)]Cl_2$	$C_{16}H_{18}N_4O_8SCl_2Cu$	560.85	65	Blue	285–286	35.46 (35.09)	3.68 (3.27)	9.73 (9.47)	79	2.85
$[Cd(Su)(Vit)]Cl_2$	$C_{16}H_{18}N_4O_8SCl_2Cd$	609.72	55	Yellow	263–265	32.68 (33.01)	3.89 (9.04)	8.97 (9.39)	72	–

Table 2: FT-IR spectral data of the ligands and the metal(II) complexes

Ligands/ Complexes	$\nu(NH_2)$	$\nu(SO_2)_{asy}$	$\nu(SO_2)_{sy}$	ν(S-N)	ν(C=N)	ν(O-H)	ν(C=O)	ν(M-N)	ν(M-O)
Sulphadiazine [Su]	3400	1339	1160	934	1649	–	–	–	–
Vitamin C [Vit]	–	–	–	–	–	3370	1717	–	–
$[Ni(Su)(Vit)]Cl_2$	3394	1351	1169	954	1670	3384	1730	572	452
$[Zn(Su)(Vit)]Cl_2$	3399	1350	1167	958	1675	3398	1738	553	439
$[Co(Su)(Vit)]Cl_2$	3394	1347	1158	942	1663	3405	1735	562	430
$[Cu(Su)(Vit)]Cl_2$	3397	1349	1169	947	1671	3425	1740	571	467
$[Cd(Su)(Vit)]Cl_2$	3409	1348	1168	953	1657	3387	1743	564	475

Table 3: Antimalarial activities of the ligands and the metal(II) complexes (Percentage reduction in parasitaemia)

Ligands/Complexes	% average parasitaemia before administration	% average parasitaemia after administration	% reduction in parasitaemia
Sulphadiazine [Su]	30	12	70
Vitamin C [Vit]	–	–	–
$[Ni(Su)(Vit)]Cl_2$	56	60	50
$[Zn(Su)(Vit)]Cl_2$	52	60	81
$[Co(Su)(Vit)]Cl_2$	48	50	76
$[Cu(Su)(Vit)]Cl_2$	50	30	77
$[Cd(Su)(Vit)]Cl_2$	55	20	89

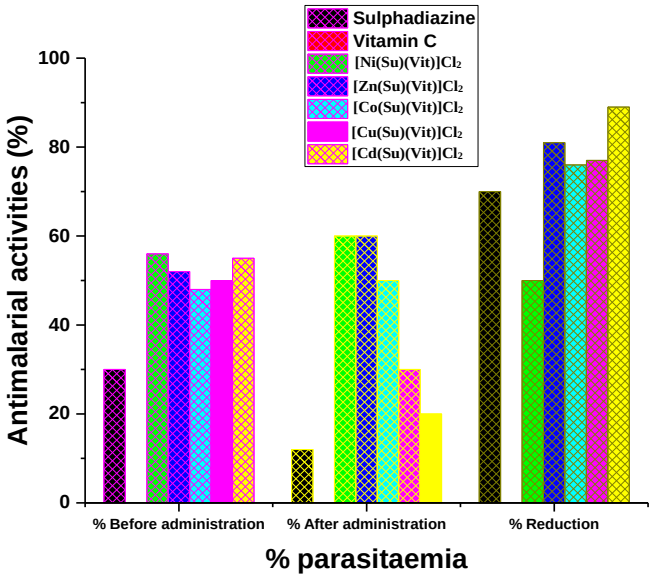


Figure 1: Antimalarial activities of the ligands and the metal(II) complexes.

Antimicrobial activities

The antimicrobial activities of the Sulfadiazine, Vitamin C, and the corresponding mixed metal complexes were evaluated against bacterial strains: *Klebsiella pneumoniae, Bacillus substilis, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa*, and *Enterococcus faecalis*. The results in Table 4 showed that the metal complexes exhibited better activities than the free ligands and such improved activity of metal chelates is characteristic of the lipophilic nature of the metal ions within the complexes sphere (Ejidike and Ajibade 2017). It also advocates that the complexes possess the antimicrobial capability of hindering the development progression of the microbes by barricading their active sites (Dikio et al. 2017, Ejidike and Ajibade 2017).

The antimicrobial activities of the ligands and their complexes are within the range of 2.5 mm to 33 mm (Figure 2). Reviewing the above-mentioned results, it is noticeable that there are different susceptibility levels between the six tested strains owing to the type of test compound. No zone of inhibition was observed for Sulphadiazine against all the bacteria strains, Vitamin C possessed action against *E. coli* and *E. faecalis*. This may be attributed to the presence of free hydroxyl groups in the latter which can react in cells leading to the initiation of the carcinogenic process. It was observed that *E. coli* was the most susceptible organism to the

ligands and complexes (Ejidike et al. 2021, Bamigboye et al. 2021a, 2021b). The presence of sulphur and nitrogen in the complexes might have helped to penetrate through the wall of the bacterial cell thereby enhancing bactericidal activities. An increase in the dipole-dipole intermolecular force between the complexes might have assisted the molecule to relate or penetrate easily through the cell membrane of the organisms (Tella and Obaleye 2010, Dikio et al. 2017, Ahmed et al. 2017, Ejidike et al. 2021). $[Zn(Su)(Vit)Cl_2]$ exhibited the highest activity (32.15 mm) against *P. aeruginosa*, while $[Cd(Su)(Vit)]Cl_2$ had the least activity with 3.09 mm.

Furthermore, the delocalization of the π-electrons increased over the entire chelate ring thus, enhancing the lipophilicity of the complexes. The lipophilic nature of the central metal ion is also increased upon complexation, which afterward favours the permeation through the lipid layer of the cell membrane, thereby obstructing the active sites, which restricts further growth of the organisms (Ejidike and Ajibade 2017, Ejidike et al. 2021, Bamigboye et al. 2021a, 2021b). The higher antimicrobial activities observed for the metals complexes could also be related to the fact that the complexes induce oxidative stress within the bacterial cell, playing an imperative character by damaging biochemical polymers such as DNA, RNA, proteins, and carbohydrates (Siddiqi et.al. 2018, Ejidike et al. 2021, Bamigboye et al. 2021b). The high activities of $[Zn(Su)(Vit)]Cl_2$ against *B. subtilis*, *E. coli*, *S. aureus*, and *P. aeruginosa* (Figure 2) could be attributed to the fact that Zn^{2+} ions released during its interaction reacts with biomolecules and inhibit multiple cellular functions of bacteria. The the antimicrobial activities of the metal(II) complexes of Sulfadiazine–Vitamin C against the investigated strains followed the following orders:

For *E. coli*:
$[Zn(Su)(Vit)]Cl_2$ > $[Co(Su)(Vit)]Cl_2$ > $[Ni(Su)(Vit)]Cl_2$ > $[Cd(Su)(Vit)]Cl_2$ > [Vitamin C] > $[Cu(Su)(Vit)]Cl_2$.

For *E. faecalis*:
$[Ni(Su)(Vit)]Cl_2$ > $[Cu(Su)(Vit)]Cl_2$ > $[Zn(Su)(Vit)]Cl_2$ > $[Co(Su)(Vit)]Cl_2$ > [Vitamin C].

For *P. aeruginosa*:
$[Zn(Su)(Vit)]Cl_2$ > $[Co(Su)(Vit)]Cl_2$ > $[Cu(Su)(Vit)]Cl_2$ > $[Ni(Su)(Vit)]Cl_2$ > $[Cd(Su)(Vit)]Cl_2$.

For *K. pneumoniae*:
$[Ni(Su)(Vit)]Cl_2$ > $[Zn(Su)(Vit)]Cl_2$ > $[Cd(Su)(Vit)]Cl_2$ > $[Cu(Su)(Vit)]Cl_2$ > $[Co(Su)(Vit)]Cl_2$.

For *S. aureus*:
$[Zn(Su)(Vit)]Cl_2$ > $[Ni(Su)(Vit)]Cl_2$ > $[Co(Su)(Vit)]Cl_2$ > $[Cu(Su)(Vit)]Cl_2$.

For *B. subtilis*:
$[Zn(Su)(Vit)]Cl_2$ > $[Co(Su)(Vit)]Cl_2$ > $[Ni(Su)(Vit)]Cl_2$ > $[Cu(Su)(Vit)]Cl_2$.

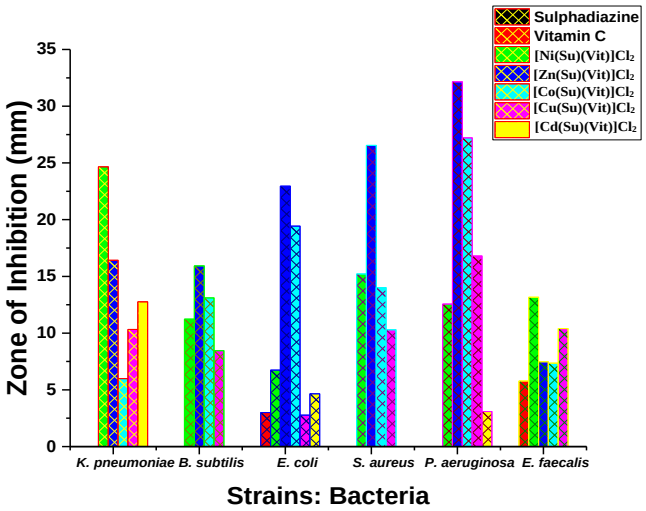


Figure 2: Antimicrobial activities of the ligands and the metal(II) complexes.

Table 4: Antibacterial activities of the ligands and the metal(II) complexes

Ligands/Complexes	Zones of inhibition (mm)					
	K. pneumoniae	*B. subtilis*	*E. coli*	*E. coli*	*P. aeruginosa*	*E. faecalis*
Sulphadiazine [Su]	–	–	–	–	–	–
Vitamin C [Vit]	–	–	3.00	–	–	5.78
$[Ni(Su)(Vit)]Cl_2$	24.66	11.23	6.74	15.21	12.56	13.16
$[Zn(Su)(Vit)]Cl_2$	16.42	15.93	22.95	26.55	32.15	7.47
$[Co(Su)(Vit)]Cl_2$	5.99	13.11	19.43	14.01	27.21	7.35
$[Cu(Su)(Vit)]Cl_2$	10.32	8.45	2.77	10.29	16.80	10.40
$[Cd(Su)(Vit)]Cl_2$	12.76	–	4.65	–	3.09	–

Relative acid stability and thermal stability

Based on the data observed in the absorbance of the complexes and the free ligands at different temperatures and pH, the absorbance changes are significant in the parent drugs but not in the complexes (Tables 5–7). This is due to the high concentrations of the complexes. This can also indicate that the ligands are less stable than the complexes, displaying more stability (Pouralimardan et al. 2017). $[Co(Su)(Vit)]Cl_2$ exhibited the highest aqueous solubility with a value of 4.07 g/dm^3. The aqueous stability of the Sulphadiazine, Vitamin C and the metal(II) complexes can be arranged as follows: [Vitamin C] > $[Co(Su)(Vit)]Cl_2$ > $[Cu(Su)(Vit)]Cl_2$ > $[Zn(Su)(Vit)]Cl_2$ > [Sulphadiazine] > $[Cd(Su)(Vit)]Cl_2$ > $[Ni(Su)(Vit)]Cl_2$ > [Sulphadiazine].

Table 5: Aqueous stability of the Sulphadiazine, Vitamin C and the metal(II) complexes

Ligands/ Complexes	Solubility (g/dm^3)
Sulphadiazine [Su]	1.33
Vitamin C [Vit]	5.27
$[Ni(Su)(Vit)]Cl_2$	1.00
$[Zn(Su)(Vit)]Cl_2$	2.80
$[Co(Su)(Vit)]Cl_2$	4.07
$[Cu(Su)(Vit)]Cl_2$	3.13
$[Cd(Su)(Vit)]Cl_2$	1.27

Table 6: Relative thermal stability of Sulphadiazine, Vitamin C, and the metal(II) complexes

Ligands/ Complexes	10 °C	15 °C	20 °C	25 °C	30 °C	λ_{max}
Sulphadiazine [Su]	0.14	0.66	0.49	0.32	0.79	385
Vitamin C [Vit]	0.28	0.13	0.31	0.75	0.41	314
$[Ni(Su)(Vit)]Cl_2$	0.71	0.62	0.63	0.19	0.33	478
$[Zn(Su)(Vit)]Cl_2$	0.36	0.17	0.10	0.12	0.59	429
$[Co(Su)(Vit)]Cl_2$	0.46	0.51	0.66	0.36	0.15	450
$[Cu(Su)(Vit)]Cl_2$	0.11	0.26	0.18	0.56	0.08	408
$[Cd(Su)(Vit)]Cl_2$	0.36	0.30	0.73	0.13	0.17	467

Table 7: Relative acid stability of Sulphadiazine, Vitamin C, and the metal(II) complexes

Ligands/Complexes	pH 1	pH 2	pH 3	pH 4	pH 5	λ_{max}
Sulphadiazine [Su]	0.39	0.21	0.92	0.18	0.64	348
Vitamin C [Vit]	0.17	0.82	0.45	0.51	0.98	337
$[Ni(Su)(Vit)]Cl_2$	0.42	0.91	0.59	0.57	0.46	394
$[Zn(Su)(Vit)]Cl_2$	0.65	0.81	0.64	0.79	0.81	372
$[Co(Su)(Vit)]Cl_2$	0.73	0.74	0.32	0.37	0.79	398
$[Cu(Su)(Vit)]Cl_2$	0.61	0.39	0.72	0.47	0.37	365
$[Cd(Su)(Vit)]Cl_2$	0.42	0.57	0.28	0.56	0.81	379

Conclusion

Some new complexes of mixed Sulfadiazine–Vitamin C have been synthesized in a ratio of 1:1:1 and characterized using various spectroscopic techniques. Spectroscopic data revealed that the ligands coordinate as a bidentate agent and forms mononuclear complexes with the Ni(II), Zn(II), Co(II), Cu(II), and Cd(II) metal ions via the nitrogen atoms of azomethine and amine groups of Sulphadiazine and oxygen atoms of hydroxyl and carbonyl groups of Vitamin C. The complexes assumed distorted tetrahedral geometries for the metal ions environment except for copper ion which assumed a square planner geometry. Based on the activity of antimalarial, $[Cd(Su)(Vit)]Cl_2$ exhibited the highest growth inhibitory activity against *Plasmodium berghei* than other complexes. The antibacterial activities against the bacteria strains: *K. pneumoniae, B. substilis, E. coli, S. aureus, P. aeruginosa*, and *E. faecalis* showed that the as-synthesized metal(II) complexes exhibited better activities than the free ligands, an indication of a broad antibacterial spectrum. Coordination of the free ligands to the central metal ions increased the antimalarial and antimicrobial activities of the complexes, thus supporting the compounds as potential chemotherapeutic agents against infectious diseases.

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Ethical Approvals

The guidelines governing the laboratory animal's use as spelled out by the Committee on Ethics for Medical and Scientific Research, the University of Ilorin, Nigeria was fully observed by the authors. Also, the standing internationally documented ideologies for laboratory animal use and care as described in the Canadian Council on Animal Care Guidelines and Protocol Review were equally practiced.

Competing Interest:

The authors proclaim that they have no conflict of interest.

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