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Afr. J. Biomed. Res. Vol. 27 (May 2024); 349- 357

Research Article

In vitro Anti-microbial and Free Radical Scavenging Activity of Zinc(II), Copper(II), Cobalt(II) and Cadmium(II) Ions Coordinated with N-(pyridin-4-yl)(tolu-4-yl)sulphonamide

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ABSTRACT

The rising use of antibiotics and antioxidants in medicine and animal care has primarily contributed to antibiotic-resistant microbes, decreased oxidative stress, and prompted the hunt for novel and effective medications. This study reports the synthesis, bioactivity, and radical scavenging potential of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide coordinated with zinc (II), copper (II), cobalt (II), and cadmium (II) ions. The condensation reaction of 4-aminopyridine and tosyl chloride produced the sulphonamide derivative. The complexes were synthesized by the reaction of ZnCl2 /Cu(NO3)2.6H2O, Co(NO3)2.6H2O, Cd(NO3)2.6H2O with the sulphonamide derivative. The antimicrobial analysis was conducted via the conventional method, and the free radical scavenging activity was achieved through the use of a 2,2-diphenyl-1-picrylhydrazyl (DPPH) solution. These compounds were characterized by physicochemical analysis, UV-VIS, FT-IR, NMR (1H and 13C) and LC-MS. The ligand and its new complexes were tested against gram (-) *Escherichia coli*, gram (-) *Salmonella typhi*, gram (+) *Staphylococcus aureus*, *Aspergillus flavus*, *Aspergillus niger*, and *Saccharomyces cerevisiae*. The findings revealed that some of the complexes have significant activity against some pathogens and show good free radical scavenging activity. The heterocyclic pyridine nitrogen in the sulphonamide is a good site for complaxation, and the methods employed and the synthesized compounds are viable sources of knowledge for the chemical and pharmaceutical industries. The study recommends further investigation into the formation of new complexes and their bioactivity with other clinical pathogens.

Keywords: *Bioactivity, Complexation, N-(pyridin-4-yl)(tolu-4-yl)sulphonamide, Synthesis.*

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Received: January 2024; Accepted: March 2024

DOI: https://doi.org/10.4314/ajbr.v27i2.21

INTRODUCTION

The incidence of bacterial and fungal illnesses' resistance to traditional antibiotic treatment, together with the emergence of multidrug-resistant pathogens, is increasing rapidly and causing concern. The problem has become a notable public health concern in medical settings, mostly due to the challenges in managing bacterial infections, the restricted access to suitable treatments, and the lack of effective preventive measures (Asfaw *et al*., 2020; Orie *et al*., 2021a). Bacteria utilize the formation of a biofilm as a crucial defence mechanism against antibiotics. The biofilm matrix has a phenotypic ability to endure different effects of antibiotics (Morehead & Scarbrough, 2018; Orie *et al*., 2021a). Based on this data, metal complexes have been acknowledged as a highly effective approach widely utilized as therapeutic agents for treating various human diseases, such as infection, diabetes, anti-inflammatory conditions, and neurological disorders (Don-Lawson *et al*., 2020; Khan *et al*., 2020). The ability of bioactive substances to act as antibiotics and antioxidants is crucial for mitigating the oxidative stress caused by disease or medication. Several investigations have shown that heterocyclic and coordinated complexes exhibit antioxidant and immunostimulatory properties (Hossain *et al*., 2018).

Free radicals are intrinsically unstable molecules generated during normal cellular metabolism (the biochemical reactions taking place within a cell). They possess the capacity

to collect inside cells and cause damage to other molecules. Active oxygen species (ROS) like superoxide, hydrogen peroxide, and hydroxyl radicals are all made from oxygen (Mei & Ming, 2008; Bhattacharya, 2015; Sani *et al*., 2017). In normal physiological conditions, aerobic cells continuously produce reactive oxygen species (ROS) and remove them using their own antioxidant defence system. Nevertheless, under pathological conditions, the balance between reactive oxygen species (ROS) and the body's antioxidant defence mechanisms is altered (Sani *et al*., 2017). Overproduction of reactive oxygen species (ROS) and other unstable chemicals can damage cellular proteins, carbohydrates, lipids, and DNA. Oxidative stress can lead to the development of several diseases, such as liver cirrhosis, inflammation, atherosclerosis, diabetes, cancer, neurological diseases, nephrotoxicity, and the ageing process. Antioxidants have the ability to prevent these oxidative damages and, hence, decrease the disturbances to homeostasis caused by free radicals.

The chemical N-(pyridin-4-yl)(tolu-4-yl)sulphonamide is an important compound that consists of the sulphonamide functional group, 4-aminopyridine, and benzene derivatives. These particular elements have been employed either alone or in combination in the pharmaceutical industry as a basis for developing drugs and catalysts or as catalysts or drugs for environmental applications.

4-aminopyridine has been employed as a precursor in the synthesis of amidine sulphonamides and benzene sulphonamides (Bhattacharya, 2015; Sani *et al*., 2017). N–(2–hydroxybenzylidene) In 2015, Abdul-Qadir *et al*. conducted a study on the chemical known as pyridine–2–amine. The mentioned compounds include N-(anthracene-9-ylmethylene)-pyridine-2-amine (Vidya, 2016) and 4-amino-1-(2-(4-bromophenyl)-2-oxethyl) pyridine-1-ium bromide (Sumrra *et al*., 2020). This drug, due to its extensive pharmacological and medical knowledge, is commonly used as a targeted inhibitor of Kv channels in clinical settings to enhance neurological conduction in people diagnosed with multiple sclerosis. By inhibiting the function of the exposed potassium (K+) channels, it enhances the process of conduction (Methew *et al*., 2021).

4-aminopyridine has a substantial impact on the production of transition metal molybdates. It acts as a buffer and forms weaker complexes with the transition metals, as observed in a study by Abdul-Qadir *et al*. in 2015. The nitrogen atom in the pyridine ring often functions as a monodentate Lewis base ligand (Hossain *et al*., 2018). Some reports have used 4-aminopyridine and its derivatives as ligands in various complexes. These include 4-aminopyridinium, 3-(4-aminopyridinium) succinate tetrahydrate hydrate (Sani & Iliyasu, 2018), (4-(amino)pyridine/4-(dimethylamino)pyridine (Prabhakaran *et al*., 2004), new [CdCl2(4-aminopyridine)2]n metal (Ostrowski & Ford, 2009), and polymer [Cu(C2O4)(4-aminopyridine)2(H2O)]. The compound n is referred to as N-(2-Hydroxy-5-nitrophenyl)-2,4,6-triisopropylbenzene sulphonamide in the study conducted by Kinali-Demirci *et al*. in 2013. Additionally, Kartal and Sahin (2021) also identified this compound by the same name.

The complexes made when 4-aminopyridine is mixed with metal ions are more biologically active than the metal ions and ligands alone when they are not bound together. According to Tweedy's idea, chelation decreases the polarity of metal ions and increases the lipophilicity of the complexes. This concept enhances the capacity of compounds to traverse the lipid membranes of bacteria and intensifies their biological efficacy (Bhattacharya, 2015; Kartal & Sahin, 2021).

The tosyl derivative is another significant motif of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide. It plays a crucial role in organic reactions due to its ability to function as a protecting group, an activator for a weak leaving group, and a precursor for synthetic intermediates used in the production of various biologically active compounds, including pharmaceuticals, herbicides, dyes, and pigments (Amalraj *et al*., 2017). The therapeutic effects of the tosyl group in medicinal chemistry are likely attributed to its rigid chemical structure, the functionality of the sulphonyl group, and its capability to engage in hydrogen bond interactions with a specific residue in the active site of biological targets. The particular arrangement assumed by this group in order to match an active site is linked to the existence of the central ring structure that restricts the side chain (Sani *et al*., 2017; Amalraj *et al*., 2017). The ability of microbes to develop resistance to commonly available antibiotics has prompted several researchers to focus on synthesising chemical compounds using readily accessible resources. In drug design and discovery, it is crucial to create a carbon framework by either removing or modifying functional groups in a manner that provides the desired functionality of the compound or target medication (Mai & Mei & Ming, 2008; Hossain *et al*., 2018). The production of sulphonamide derivatives from both carbocyclic and heterocyclic chemicals is a significant category of pharmaceuticals that possess diverse pharmacological properties and are utilised in contemporary medicinal science. The expansion of this category of medications has resulted in the consecutive advancement of enhanced antibiotics, pharmaceuticals that stimulate insulin release, anti-hypertensive therapies, and so on (Mei & Ming, 2008; Sani *et al*., 2017). The sulphonamide derivatives of 4-aminopyridine serve as a prototype for the N-heterocyclic molecule of interest.

Some of the sulphonamides used in complexes are (4-{E-[(2-hydroxy-3-methoxyphenyl)methylidene]amino}benzene-1-sulphonamide and 4-{[(2-hydroxy-3-methoxyphenyl)methylidene]amino}-N-(5-methyl-1,2-oxazol-3-yl)benzene-1-sulphonamide (Donlawson *et al*., 2020), 4-amino-N-(5-methyl-3-isoxazolyl)benzene sulphonamide (Pervaiz *et al*., 2020), N-(quinolin-8-yl)-4-chloro-benzenesulphonamide cadmium (II) (Bernardi *et al*., 2008), N-(pyridin-2-yl-methyl)biphenyl-4-sulphonamide and N-bis-(pyridin-2-yl-methyl)biphenyl-4-4'-sulphonamide(Diaconu *et al*., 2020), 4-methyl-N-(pyridin-2-yl)benzenesulphonamide (Bodoki *et al*., 2020). Sulphonamides and their derivatives possess antibacterial and anticancer activities, along with anti-carbonic anhydrase, antithyroid, hypoglycemic, and protease inhibitor capabilities (Mei & Ming, 2008; Sani *et al*., 2017; Donlawson *et al*., 2020).

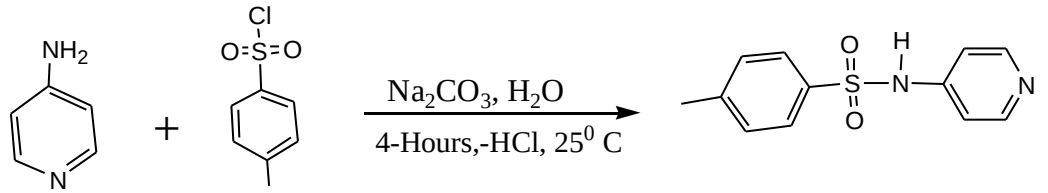
These compounds have gained recognition in the fields of bio-inorganic and metal-based drug chemistry due to their significant pharmacological applications. The growing interest in organometallic medicinal chemistry has led to the meticulous design and synthesis of metal-based sulphonamides with promising therapeutic properties. The aim of the study is to synthesize N-(pyridin-4-yl)(tolu-4-yl)sulphonamide by the reaction of 4-aminopyridine and tosyl chloride. This compound undergoes complexation with Zn(II), Cu(II), Co(II), and Cd(II). The efficacy against disease-causing microorganisms and the ability to prevent oxidation were evaluated using a solution of 2,2-diphenyl-1-picrylhydrazyl (DPPH).

MATERIALS AND METHODS

Materials and Equipment: The chemicals include sodium trioxocarbonate (IV), acetic acid (AA), tosyl chloride ethanol (EtOH), 4-aminopyridine, and others. TLC was performed on a Merck pre-coated silica gel plate (10 x 10 cm), and the Rf value was determined with a solvent mixture. A 256 nm UV lamp was used to view the chromatogram. A Digital Melting Point Electrothermal IA9300X1 was used to measure the melting point. The IR spectra were analyzed at NARICT Zaria, Nigeria, using an ATR disc and a Fourier transform infrared spectrophotometer (FTIR-8400S). At the University of Strathclyde in the United Kingdom, Liquid Chromatography/Mass Spectrometry, Proton Nuclear Magnetic Resonance (1HNMR), and Carbon-13 Nuclear Magnetic Resonance (13CNMR) were all recorded in DMSO in Spectrophotometer. The electronic spectra between 200 and 600 nm were acquired in DMSO using a UV-1800 Shimadzu UV-Vis Spectrophotometer at ambient temperature. The mass spectra were collected in acetonitrile using a Shimadzu LCMS 2020 instrument.

Experimental Methods

Synthesis of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide: The synthesis of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide was conducted with minor adjustments to the techniques described by Abdul-Qadir *et al*. (2015) and Rehman *et al*. (2017). In an Erlenmeyer flask of 500 ml capacity, sodium trioxocarbonate (IV) (1M, 20 ml) and 4-aminopyridine (5 g, 0.053 mol) were placed in distilled water (25 ml). For 15 minutes, the mixture was vigorously stirred using an electromagnetic stirrer. The solution was then vigorously stirred at room temperature for 4 hours in a fume compartment while tosyl chloride (10 g, 0.053mol) was added gradually. The change of the pH from alkaline to acidic signified the conclusion of the reaction, and TLC analysis revealed that the majority of the initial materials had been depleted. In order to achieve a pH of 2, a few droplets of concentrated hydrochloric acid were introduced. This modification induced precipitation of the product, which was subsequently filtered and collected. The reaction was carried out at room temperature (250C) in a fume chamber. Following multiple washes with distilled water, the resulting solid was recrystallized using a 1:5 mixture of ethanol and water as the solvent system. This resulted in the formation of an off-white solid, which was subsequently desiccated at room temperature and characterized. The UV-Vis spectrum is summarized in Table 2 and reaction in Scheme 1 depicts the synthesis of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide, [Cu(C12H12N2O2S)2], Yield: 50% (0.50g); off-white solid, Rf 0.80, AA:EtOH:H2O, 2:1:1); 210-212 oC, IR (ATR): 3286.81, 3610.86 NH, 2918.47CH, 1689.70 C=N, 1519.96 C=C, 1134.18 C-N, 1003.03 S=O, 933.58, 846.71 aromatic C=C; 1HNMR(500 MHz, DMSO), (δ ppm) 11.03 (br, s, 1 H, NH), 8.05 (dd, J=5.63 Hz, 1.88 Hz, 2H, ArH), 7.15 (d, J=7.85.11 Hz, 2H, ArH), 7.33 (dd, J=8.03Hz, 2H, ArH), 6.91 (dd, J=6.85 Hz,5.46 Hz, 2H, ArH), 2.32(s, 3H, CH3). 13CNMR(126 MHz, DMSO), (δ ppm); 21.04, 125.85, 128.90, 139.92, 142.97. LC-MS(acetonitrile): 248.910[M+], Anal. calc. for C12H12N2O2S: C,57.85; H,4.82; N,11.24; O,12.85; S,12.61; Found: C,57.56; H,5.09; N,11.80; O,13.46; S11.89.



4 Aminopyridine Tosyl Chloride

N-(pyridin-4-yl)(tolu-4-yl)sulphonamide

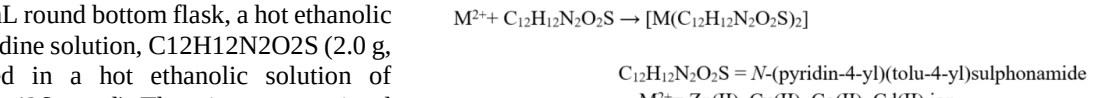
Scheme 1:
Synthesis of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide

Complexation of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide with Zinc: In a 250 mL round bottom flask, a hot ethanolic sulphonylated aminopyridine solution, C12H12N2O2S (2.0 g, 806 mmol), was placed in a hot ethanolic solution of ZnCl2 (0.55 g, 403 mmol). The mixture was stirred for 2 hours and then set aside for 2 hours. The resulting precipitate was filtered and washed many times with ethanol. The products were recrystallized in a solvent mixture of DMSO and ethanol (1:6) and dried at room temperature. The UV-Vis spectrum is summarized in Table 2 and reaction in Scheme 2 represents the complexation reaction of N-(pyridin-4-yl)tolu-4-ylsulphonamide. Yield: 57%; Rf 0.80(AA:ACE; 1:2) White solid, 200-202 oC; IR (ATR): 3294.53, 3618.58 NH, 2901.04 CH, 1666.55 C=N, 1527.67 C=N, 1003.02 S=O, LC-MS(acetonitrile): 561.40[M+],Anal. calc. of [Zn(C12H12N2O2S)2], Zn: 11.63; C, 50.79; H, 4.28; N, , 9.98 ; O 11.40; S, 11.40 Found: Zn: 4. 48 ;11.63; C51.30,; H, 4. 48; N, 9.98; O, 11.66; O 11.58.

Complexation of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide with Copper: In a 250 mL round bottom flask, a hot ethanolic sulphonylated aminopyridine solution, C12H12N2O2S (2.0 g, 806 mmol), was placed in a hot ethanolic solution of Cu(NO3)2.6H2O (1.26 g, 426 mmol). The mixture was stirred for 2 hours and then set aside for 2 hours. The resulting precipitate was filtered and washed many times with ethanol. The products were recrystallized in a solvent mixture of DMSO and ethanol (1:6) and dried at room temperature. The UV-Vis spectrum is summarized in Table 2 and reaction in Scheme 2 represents the complexation reaction of N-(pyridin-4-yl)tolu-4-ylsulphonamide [Cu(C12H12N2O2S)2] (Scheme 2);Yield: 60% ;Rf 0.83(AA:ACE ;2:1) Blue solid, 213-215 oC; IR (ATR): 3294.53, 3610.55 NH, 2931.90 CH, 1674.27 C=N, 1134.18 C – N S=O, 1010.73, 848.71 Aromatic C=C, 1519.95 C=C; LC-MS(acetonitrile): 560.3956[M+], Anal. calc. for C12H12N2O2S: Cu: 11.42; C, 51.40; H, 4.28; N, 10.00; O, 11.43; S, 10.42 Found: Zn:11.55; C52.37; H, 4. 62; N, 10.27; O, 10.55; S, 10.64.

Complexation of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide with Cobalt: In a 250 mL round bottom flask, a hot ethanolic sulphonylated aminopyridine solution, C12H12N2O2S (2.0 g, 8.06 mmol), was placed in a hot ethanolic solution of Co(NO3)2.6H2O (1.17 g, 4.02 mmol). The mixture was stirred for 2 hours and then set aside for 2 hours. The resulting precipitate was filtered and washed many times with ethanol. The products were recrystallized in a solvent mixture of DMSO and ethanol (1:6) and dried at room temperature. The UV-Vis spectrum is summarized in Table 2 and reaction in scheme 2 represents the complexation reaction of N-(pyridin-4-yl)tolu-4-ylsulphonamide, [Co(C12H12N2O2S)2] (Scheme 2);Yield: 57% ;Rf 0.75 (AA:ACE(1:2), Yellow solid, 184-186 oC; IR (ATR): 3356.25, 3603.15 NH, 2931.30 CH, 1651.12, C=N, 1519.06 C=C, 1134.18 C – N, 1010.73 S=O, 925.88, 840.99 aromatic C=C; LC-MS(acetonitrile): 555.1335[M+], Anal. calc. for ,[Co(C12H12N2O2S)2] : Co: 10.39; C, 51.75; H, 4.31; N, 10.06; O, 11.50; S, 11.50, Found: Co: 10.75 ; C 50.35; H, 4.96; N, 10.49; O, 11.72; S, 11.73.

Complexation of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide with Cadmium: In a 250 mL round bottom flask, a hot ethanolic sulphonylated aminopyridine solution (2.0 g, 8.06 mmol) was put in a boiling ethanolic solution of Cd(NO3)2.6H2O (1.39 g, 4.04 mmol). The mixture was agitated for 2 hours and left to stand for 2 hours. The precipitate that developed was filtered and washed many times with ethanol. The products were recrystallized in a solvent mixture of DMSO and ethanol (1:6) and allowed to dry at room temperature. The UV-Vis spectrum is summarized in Table 2 and reaction in scheme 2 represents the complexation reaction of N-(pyridin-4-yl)tolu-4-ylsulphonamide,[Cd(C12H12N2O2S)2]; Yield: 60%; Rf 0.84 (AA:ACE(1:2), White solid, 208-210 oC; IR (ATR): 3286.81, 3610.84 NH, 2931.90 CH, 1615.12 C=N, 1519.99 C=C, 1134.18 C – N, 1010.73 S=O, 925.86, 840.99 aromatic C=C; LC-MS(acetonitrile): 608.9856[M+], Anal. calc. for [Co(C12H12N2O2S)2] Co: 18.42; C, 47.17; H, 3.93; N, 9.20); O, 10.45; S, 10.48, Found: Cd: 17.67; C 48.03; H, 4.50; N, 9.06; O, 10.06; S, 10.68.



Scheme 2:
Complexation of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide

Pathogen Isolation: The pathogens for the bioactivity of this study were three bacteria strains (gram (-) Escherichia coli, gram (-) Salmonella typhi, and gram (+) Staphylococcus aureus) and three fungi strains (Aspergillus flavus, Aspergillus niger and Saccharomyces cerevisiae). These pathogens were isolated and confirmed in the Department of Microbiology, University of Port Harcourt. The antimicrobial activities of the ligands and their complexes were investigated using the well diffusion. The bioactivity experiment was a positive control, since both standard antibiotic and the compound synthesized was subjected to the same condition.

Antimicrobial Test Agent Preparation: The antimicrobial test agents, including both ligand and complexes, were prepared at various concentrations (1000, 500, 250, 125, 62.5, and 31.25 mg/mL) using the serial dilution method. The dilutions were made in sterile test tubes containing 50% v/v DMSO, and each tube was suitably marked (Zahan *et al*., 2015).

Bacteria Sensitivity Test: The compounds were evaluated against Gram (-) E. coli, Gram (-) S. typhi, and Gram. (+) S. aureus. The medium was created in accordance with the manufacturer's specifications. A cork borer was sterilised by soaking it in ethanol, then passing it through a Bunsen flame before being used to make wells in the media. In the wells, several dilutions of the bioactive substances produced with 50% DMSO were injected (Donlawson *et al*., 2020). The Petri dishes were incubated at 37 °C for 18-24 hours. Finally, the plates were examined, and the diameter of the zone of inhibition around the well in millimetres (mm) was measured. The experiment was done in triplicates and mean was used to estimate the value in Table 3.

Fungal Sensitivity Test: *A. Flavus*, *A. niger*, and *S. cerevisiae* were used to examine the synthesised chemicals. This test was conducted using the well-in-agar diffusion method with Dextrose Agar, as recommended by Pervaiz *et al*. (2020). The fungal isolates were cultured at room temperature for 120 hours after being refreshed on a freshly prepared medium. The spores were taken from a well-sporulated colony and placed in a tube of sterile distilled water before being added to the molten medium, gently agitated to homogenise, poured into sterile Petri dishes, and allowed to solidify. To construct wells in the medium, a cork borer was employed, and multiple dilutions of the bioactive compounds produced with dimethyl sulphoxide (DMSO) were put into the wells (5mm in diameter). For 5-7 days, all infected plates were incubated at room temperature. Thereafter, plates were observed for the zones of inhibition around the wells. The experiment was conducted in triplicate, and the mean was used to estimate the value in Table 3.

DPPH radical scavenging assay: The radical-scavenging activity of the ligand and its complexes was determined using the method published by Bernardi *et al*. (2008). In brief, 1 mL of the sample (12.5, 25, and 50 mg/mL) was added to 1 mL of a 2,2-diphenyl-1-picrylhydrazyl (DPPH) solution (0.2 mM in methanol) as the free radical source and maintained at room temperature for 30 minutes. The decrease in solution absorbance caused by the ligand's and its complexes' proton-donating activity was measured at 517 nm. Vitamin C was used as the positive control. The percentage DPPH radical scavenging activity was calculated using the following formula:

% DPPH radical scavenging activity= {(A0− A1)/A0} ×100%
Where A0 is the absorbance of the control, and A1 is the absorbance of the ligand/complexes. The experiment was repeated three times at each concentration.

RESULTS

The result of synthesis, bioactivity and radical scavenging potential of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide coordinated with Zinc (II), Copper (II), Cobalt (II) and Cadmium (II) ions are shown in Table 1-3.

Table 1:
Selected UV-VIS Absorption Bands for N-(Pyridin-4-yl)(tolu-4-yl)sulphonamide and complexes.

compounds	Adsorption nm	ε (Lmol^{-1},cm^{-1})	Band assignment	Molar conductivity $\Omega^{-1}cm^{-2}mol^{-1}$
$C_{12}H_{12}N_2O_2SN_2O_2S$	**218, 220, 256**	**2198, 786,2330**	**$\pi \rightarrow \pi^*$,n $\rightarrow \pi^*$**	**8.5**
[Zn($C_{12}H_{12}N_2O_2S)_2$]	**375–307**	**440, 1333**	**$\pi \rightarrow \pi^*$, n $\rightarrow \pi^*$**	**10.2**
[Cu($C_{12}H_{12}N_2O_2S)_2$]	**410–307,**	**2237, 1678**	**$\pi \rightarrow \pi^*$, n $\rightarrow \pi^*$**	**12.5**
[Co($C_{12}H_{12}N_2O_2S)_2$]	**390-315**	**1583, 1890**	**$\pi \rightarrow \pi^*$, n $\rightarrow \pi^*$**	**12.0**
[Cd($C_{12}H_{12}N_2O_2S)_2$]	**300-274**	**2.324, 1760**	**$\pi \rightarrow \pi^*$, n $\rightarrow \pi^*$**	**11.5**

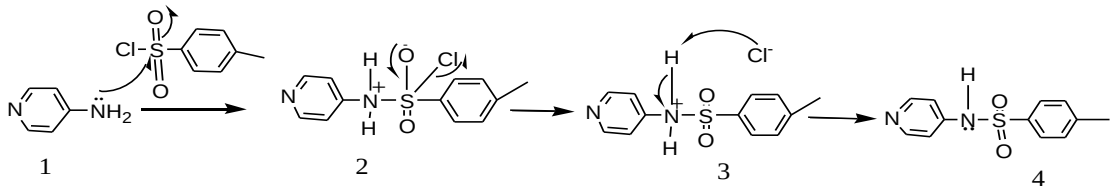
$\pi \rightarrow \pi^*$, n $\rightarrow \pi^*$, Electronic transition from highest occupy molecular orbital(HOMO) to Lowest unoccupy molecular orbital(LUMO)

Table 2:
Activity of Tosylated Aminopyridine and its complexes against some bacteria and fungi strains

variables	Antibacterial activity			Antifungal activity		
	Zone of inhibition (mm)					
	Gram(-)		Gram (+)	Fungal		
compounds	*E. coli*	*S typhi,*	*S aureus,*	*A flavus*	*A niger*	*S cerevisaea*
$C_{12}H_{12}N_2O_2S$	-	-	-	-	-	-
[Cu ($C_{12}H_{12}N_2O_2S)_2$]	5	12	10	6	12	30
[Zn ($C_{12}H_{12}N_2O_2S)_2$]	-	-	-	-	6	10
[Co($C_{12}H_{12}N_2O_2S)_2$]	20		26	28	-	16
[Cd($C_{12}H_{12}N_2O_2S)_2$]	25	9	-	12	-	20
Ciprofloxacin	34	36	36	-	-	-
ketoconazol	-	-	-	20	26	16

Table 3:
In-Vitro Free Radical Scavenging Activity

Compds	% inhibition 50 mg / mL	% inhibition 25 mg/mL	% inhibition 12.5 mg/mL
$C_{12}H_{12}N_2O_2S$	81.17 ±0.31	86.60 ± 0.22	70.96 ± 0.32
[Cu ($C_{12}H_{12}N_2O_2S)_2$]	78.40 ± 0.12	80.10 ± 0.30	64.14 ± 0.26
[Zn ($C_{12}H_{12}N_2O_2S)_2$]	75.50 ±0.42	77.33 ± 0.31	78.23 ± 0.18
[Co($C_{12}H_{12}N_2O_2S)_2$]	75.50 ± 0.66	87.68 ± 0.21	67.42 ± 0.18
Vitamin C	88.98 ±0.44	91.68 ± 0.40	92.44 ± 0.41



Scheme 3: Mechanism of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide

DISCUSSION

N-(pyridin-4-yl)(tolu-4-yl)sulphonamide was synthesized by the reaction of an equal mole of tosyl chloride and 4-aminopyridine in aqueous alkaline medium at room temperature. It was used after purification for the preparation of the complexes of Cu(II), Zn(II), Cd (II) and Co(II) at ambient temperature. The mechanistic design for the synthesis of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide is shown in Scheme 3 and was in agreement with Lakrout *et al*. (2014) and Orie *et al*. (2021b), which worked on the tosylation of aniline using different solvents.

The melting points of the ligand and the complexes are within the range of purity. This is further affirmed by the data from the TLC investigation with a single spot in the different solvent systems used as mobile phases. Abdul-Qadir *et al*. (2015) estimated a melting point range of 178–180 oC and an Rf value of 0.72 for the synthesis of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide, which is an isomer of monotosylated 4-aminopyridine derivatives. The changes in melting point range and Rf value could be associated with the different isomers of the aminopyridine used as the substrate. In the study by Orie *et al*. (2021b), the monotosylated 4-aminopyridine also has a melting point range that matches N-(pyridin-4-yl)(tolu-4-yl)sulphonamide.

The ligand was found to be soluble in ethanol (EtOH), acetic acid (AA), dimethyl formamide (DMF), and dimethyl sulphoxide (DMSO), but insoluble in water (H2O), hexane (Hex), acetone (Ace), and ethyl acetate (EA) (Zhang *et al*., 2020; Orie *et al*., 2020c). The development of a hydrogen bond was connected with the solubility of both the ligand and complexes in the solvent (Ostrowski & Ford, 2009; Sultana *et al*., 2010).

The ligand and complexes' suggested formula was well supported by the elemental analysis data acquired from the LC-MS molecular masses. According to the LCMS extrapolation, the masses of Cu(II), Cd(II), Co(II), and Zn(II) were estimated at 560.3959, 608.9856, 555.1335, and 561.4044, respectively, and were consistent with the proposed molecular masses. This shows that the coordinated compounds were pure and effective because the percentage compositions of the components in the complexes' experimental and calculated mass formulae were quite consistent. The findings show a metal-to-ligand chelation ratio of 1:2 (M:2L). Findings from the ligand's elemental analysis are in agreement with previous studies on montosylated 4-aminopyridine (e.g., Abdul-Qadir *et al*., 2015; Orie *et al*., 2020c). The conductivity of the complexes revealed that all the complexes are non-electrolytes by nature. The obtained values imply that no anion is present outside the coordination sphere in all the complexes (Tsapkov *et al*., 2008; Hossain *et al*., 2018).

1H NMR spectra displayed signals assigned to the sulphonamide (O=S-N-H) at 11.03 ppm (1H, s) in DMSO solvent, which confirms the condensation of reactants. Previous research by Abdul-Qadir *et al*. (2015) reported the sulphonamide proton to be 11.45 ppm in a deuterated ethanol solvent. Orie *et al*. (2020c) assigned 12.40 ppm to the proton of sulphonamide with 2-aminopyridine in a DMSO solvent. The difference in the chemical shift proton of sulphonamide could be attributed to different solvents used in the 1H NMR analysis and different substituents in sulphonamide derivatives. The chemical shift range of 6.95–7.47 ppm is within the aromatic zone of the 1H NMR spectrum. Similar research by Zahan *et al*. (2015), Zhang *et al*. (2015), and Sumrra *et al*. (2020) conforms with the aromatic zone of 6.95–7.47 ppm. Thus, the presence of benzene and the pyridine ring of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide were confirmed. The peak with the chemical shift value of 2.11 ppm was assigned to the methyl group of toluene (Mei & Ming, 2008).

Table 1 shows the observed electronic transitions of the coordinated complexes and pure N-(pyridin-4-yl)(tolu-4-yl)sulphonamide in a DMSO solution at room temperature, spanning 200–1100 nm. The $\pi \rightarrow \pi^*$ transition of the benzene rings is represented by the band at 220-200 nm, while the absorptions at 256-248 nm were attributed to the $n \rightarrow \pi^*$ transitions of the azomethine group, HC=N of 2-aminopyridine. The transition band for ligand metal charge transfer in the Cu(II) complex was estimated to be 410–307 nm, while the prominent band for ligand metal charge transfer (LMCT) in the Zn(II) complex was estimated to be 375–307 nm. The transition band of 390–315 nm was assigned to ligand metal charge transfer in the cobalt (II) complex, and the transition band of 300–274 nm was assigned to ligand metal charge transfer in the cadmium (II) complex. These transition bands of 250–420 nm for ligand-metal charge transition (LMCT) in complexes were consistent with Hossain *et al*. (2018), who worked on the coordination of Schiff bases of 2-aminopyridine derivatives with some metal complexes. Table 1 shows the UV-VIS absorption bands for N-(pyridin-4-yl)(tolu-4-yl)sulphonamide and complexes.

The molar conductivities of the ligand and its complexes were determined in DMSO (10−3 M) at 25 oC, as shown in Table 1. N-(Pyridin-4-yl)(tolu-4-yl)sulphonamide has the conductivity of 8.5 Ω-1cm-2mol-1 . Table 1 shows that the complexes' conductivity was greater than the ligand compounds' conductivity. The results show that none of the complexes had any anions outside the coordination sphere, which further implies that the produced chemical is not electrolytic. Tsapkov and colleagues (2008)

The stretching vibration of -N-S=O (sulphonamide) was allocated to an absorption band at 11249.91 cm-1 in the ATR-FTIR spectrum study; however, in similar research, Pervaiz *et*

al. (2020) assigned 1161 cm-1 to the vibration frequency of sulphonamide. The pyridine ring's imine displayed a 1689.70 cm-1 frequency band. Mathew *et al*. (2021) conducted research on the synthesis and complexation of 4-aminopyridine derivatives, which aligns with this observation. Orie *et al*. (2021b) and Tsapkov *et al*. (2008) found that the other frequency bands were consistent with the expected product. The free ligand's infrared data was compared to that of the coordinated ligands. After the complexation, there was a change in the vibrational frequency of the imine group of 4-aminopyridine in N-(Pyridin-4-yl)(tolu-4-yl)sulphonamide. This suggests that the metal atom coordinated with the imine nitrogen. The transfer of electrons from the nitrogen atom to the metal atom's open d-orbital accounted for this. This finding aligns with the study conducted by Sani and Iliyasu (2018), which investigated the synthesis of N-(2-hydroxylbenzylidene) pyridine-2-amine and its M (II) complexes. The study observed a comparable fluctuation in the vibration frequency of free imines and coordinated metals. The vibrational frequencies of the N-Zn complex, N-Cu complex, N-Co complex, and N-Cd complex were 1666.67 cm-1, 1674.27 cm-1, 1651.12 cm-1, and 1674.27 cm-1, respectively, that are different from the absorption of the ligand's free imine group, which is 1689.70 cm-1. These results agreed with those of Orie *et al*. (2019a), who looked into how to make and combine 4-Methyl-N-(pyridin-2-yl)benzenesulphonamide, and Mathew *et al*. (2021), who looked into how to make and combine 2-aminopyridine Schiff bases. In both situations, the vibration frequency of the free imine differed slightly from that of the coordinated imine.

The synthesised compounds were tested against several clinical pathogens, and their bioactivity is presented in Table 2. The results indicate that the synthesized compounds exhibited susceptibility to certain bacteria out of the six that were examined at a concentration of 1000 mg/mL. The ligand and its complexes were inactive at other concentrations that were considered. The ligand was not active against all pathogens examined, although its complexes increased activity against certain of them.

This can be due to the fact that the complex has a higher lipophilicity compared to the ligand. The chelating theory posits that the polarity of metal atoms is diminished to a greater degree as a result of the overlapping of ligand orbitals and the partial sharing of positive charge between the metal atoms and donor atoms (Abdul-Qadir *et al*., 2015; Ijeomah & Tseeka, 2020; Okocha *et al*., 2023). In addition, they hold the belief that chelation enhances the dispersion of electrons over the entire chelate ring and augments the lipophilicity of the complex. So, it makes it easier for the complex to get into the lipid membrane and blocks the metal binding sites on the enzymes of microbes. At 1000 mg/mL, Cu(II), Cd(II), and Co(II) complexes had the maximum zone inhibition against bacterial strains. Cu (II) complex has a zone inhibition of 12 mm against Gramme (-) S typhi, Cd (II) complex has a zone inhibition of 25 mm against Gramme (-) E coli, and Cd (II) complex has a zone inhibition of 26 mm against Gramme (+) S aureus. These findings support the findings of Duru *et al*. (2014), who discovered that complexes of imidazole derivatives were more bioactive than the ligands. As a benchmark, ciprofloxacin inhibits the growth of Gram-negative E. coli by 34 mm and Gram-positive Staphylococcus aureus by 36 mm. The results indicate that the synthetic chemical was less effective against all bacterial strains compared to the standard drugs. Ijeomah and Tseeka's (2020) phenyl sulphonamide sensitivity test was in line with this observation. When compared to the synthetic molecule, the traditional medication, ciprofloxacin, performed better against Gram (+) Escherichia coli.

The Cu(II) complex exhibits a zone inhibition of 30 mm against *S. cerevisiae* , while the Co(II) complex demonstrates a zone inhibition of 28 mm against *A. Flavus*. The compound of Cu (II) and Co(II) reduced the growth of the organism more than the standard medicine (ketoconazole), which had 20 mm against *A. Flavus* and 16 mm against *S. cerevisiae* . Both complexes exhibited higher sensitivity compared to the conventional medication (Table 2). The discovery was consistent with the findings of Amalraj *et al*. (2017) and Lakrout *et al*. (2014), which indicated that sulphonamide derivatives of aniline outperformed the standard. Additional research must be conducted to examine the susceptibility to alternative infections.

Table 3 displays the in vitro free radical scavenging activity of the ligand, its complexes, and the standard. The DPPH scavenging activity assay conducted in this work demonstrated that N-(pyridin-4-yl)(tolu-4-yl)sulphonamide and its complexes exhibited strong activity. The DPPH radical is a persistent organic free radical that exhibits an absorption band within the range of 515–528 nm. Consequently, it serves as a valuable reagent for studying the free radical scavenging properties of various compounds (Bernardi *et al*., 2008). The antioxidant capacity of the ligand and complexes was significant at a concentration of 25 mg/mL but comparatively lower at concentrations of 12.5 mg/mL and 50 mg/mL. The ligand and Zn(II) complexes exhibit the maximum radical reduction potential at a concentration of 12.5 mg/mL, with values of 70.96 ± 0.32 and 78.23 ± 0.18, respectively. The data shown in Table 3 demonstrates that the radical scavenging capacity of both the ligand and complexes exhibits an upward trend as the concentration increases, with the exception of Zn(II) complexes. Interestingly, the Zn(II) complexes display a significant reduction capacity even at a low concentration of 12.5 mg/mL.

The vitamin C used as a positive antioxidant control exhibits superior radical scavenging capability compared to both the ligand and its complexes. Furthermore, the antioxidant activity intensifies as the concentration drops. The radical scavenging and reduction properties of the vitamin C and Zn(II) combination exhibit a similar pattern. The radical scavenging activity of conventional vitamin C is superior to that of N-(Pyridin-4-yl)(tolu-4-yl)sulphonamide and its complexes.

The main goal of this research is the synthesis and bioactivity of N-(pyridin-4-yl)(tolu-4-yl)sulphonamide coordinated with zinc (II), copper (II), cobalt (II), and cadmium (II) ions. N-(Pyridin-4-yl)(tolu-4-yl)sulphonamide was synthesized the action of tosyl chloride on 4-aminopyridine at room temperature. It was characterized and used as a ligand to form the complexes of Zn (II), Cu (II), Cd (II), and Co (II).

A study of the complexes shows that the metal ion coordinates with the imine nitrogen of 4-aminopyridine. The appearance of frequency bands at 1697.27 cm-1, 1666.55, 1674.30, and 1651.12 cm-1 in the spectra of imine nitrogen of 4-aminopyridine, as against 1681.98 cm-1(free ligand), suggests the formation of the new compound. The compounds were tested against Gram (-) E coli, Gram (-) S typhi and Gram (+) S aureus, *A. Flavus*, *A. niger*, and *S. cerevisiae* . The activity test revealed that some of the complexes have significant activity against some pathogens. The in vitro free radical scavenging activity of the ligand and its complexes was high. The chemical and pharmaceutical sectors can greatly benefit from the methods used, the molecules synthesized, and the in vitro free radical scavenging capabilities. The complexes should be analyzed using an ESR spectroscopic method to determine their nature, and the newly synthesized chemical should be tested against different pathogens.

Acknowledgement:
I would like to express my gratitude to the Department of Pure and Industrial Chemistry at the University of Port Harcourt, Nigeria for providing access to the laboratory and departmental library over the duration of this project.

REFERENCES

Abdul-Qadir M., Ahmed M., Aslam H., Waseem S. and Shafiq MI. (2015) Amidine sulphonamides and benzene sulphonamides: Synthesis and their biological evaluation", *Journal of Chemistry*, 2015. https://doi.org/10.1155/2015/524056

Amalraj A., Pius A., Gopi S. and Gopi S.(2017) Biological activities of curcuminoids, other biomolecules from turmeric and their derivatives–A review, . *Journal of traditional and complementary medicine*, 7(2): 205-233. https://doi.org/10.1016/j.jtcme.2016.05.005

Asfaw D., Ali B., Tadesse A. and Ebabu A.(2020) Prevalence and antibiotic resistance pattern of Salmonella isolated from caecal contents of exotic chicken in Debre Zeit and Modjo, Ethiopia. *International Journal of Microbiology*, https://doi.org/10.1155/2020/1910630

Bernardi, A. P. M., López-Alarcón, C., Aspée, A., Rech, S. B., Von Poser, G. L., Bridi, R. and Lissi, E. (2008). Antioxidant activityin southern brazil hypericum species. *Journal of the Chilean Chemical Society*, 53(4), 1658-1662.

Bhattacharya, S. (2015). Reactive oxygen species and cellular defense system. *Free radicals in human health and disease*, 17-29.

Bodoki, A., Alzuet-Pina, G., Borras, J., Topală, T., Hangan, A., Borodi, G. and Oprean L. (2020). Copper (ii) complexes with new w-substituted sulfonamides-synthesis, crystal structure and evaluation of the nuclease activity. Studia Universitatis Babes-Bolyai, Chemia, 65(1): 55-59. doi:10.24193/subbchem.2020.1.05

Diaconu, D., Mangalagiu, V., Amariucai-Mantu, D., Antoci, V., Giuroiu, C. L. and Mangalagiu, I. I. (2020). Hybrid quinoline-sulphonamide complexes (M2+) derivatives with antimicrobial activity. Molecules, 25(12): 2946. https://doi.org/10.3390/molecules25122946

Don-Lawson, C., Nweneka, D. O., Okah, R. and Orie, K. J. (2020). Synthesis, Characterization and Bioactivity of 1, 1-bis (2-Carbamoylguanidino) furan-2-ylmethane". *American Journal of Analytical Chemistry*,11(6):261-270. 10.4236/ajac.2020.116020

Duru, I.A., Ngochindo, R.I., Duru, C.E., Ogukwe, C.E. and Orji, I. (2014). Chlorinated Imidazole Complexes as Potent Antifungal Agents. *Journal of Applied Chem*, 7(9), 20-23.

Hossain, M. M., Bashar, M. A., Khan, M. N., Roy, P. K., Ali, M. S., and Farooque MA, (2018). Preparation, Physical Characterization and Antibacterial Activity of Ni (II), Cu (II), Co (II), Cd (II), Zn (II) and Cr (III) Schiff Base Complex Compounds, *Journal of Chemistry*, 6: 17-23. doi: 10.11648/j.sjc.20180602.11

Ijeomah, A. and Tseeka, M. (2020). Synthesis, characterisation and antibacterial activity of 2-(phenyl sulfonyl) amino pyridine. *Journal of Chemical Society of Nigeria*, 46(1). DOI: https://doi.org/10.46602/jcsn.v46i1.573

Kartal, S. and Sahin, O. (2021). Synthesis, X-ray crystallography characterization, and DFT theoretical studies of a new metal compound [CdCl2 (4-aminopyridine)2], *Journal of Molecular Structure*, 130720, https://doi.org/10.1016/j.molstruc.2021.130720

Khan, F., Pham, D. T., Oloketuyi, S. F. and Kim, Y. (2020). Antibiotics Application Strategies to Control Biofilm Formation in Pathogenic Bacteria, *Current Pharmaceutical Biotechnology*, 21(4):270-286. https://doi.org/10.2174/1389201020666191112155905

Kinali-Demirci, S., Demirci, S. and Kurt M.(2013). Synthesis, structure characterization and antimicrobial evaluation of 4-(substituted phenylazo)-3, 5-diacetamido-1H-pyrazoles", Spectrochimica Acta Part A: *Molecular and Biomolecular Spectroscopy* 106:12-18,. https://doi.org/10.1016/j.saa.2012.12.074

Lakrout, S., K'tir, H., Amira, A., Berredjem, M. and Aouf, N. E. (2014). A simple and eco-sustainable method for the sulfonylation of amines under microwave-assisted solvent-free conditions. RSC Advances, 4(31), 16027-16032.

Mathew, G., Francis, S., Rajak, N. K., Praveen, S. G., Tomy, C. V. (2021). A Simple Synthesis Method for Growing Single Crystals of a Copper Coordination Polymer [Cu(C 2O2)(4-aminopyridine) 2 (H2O)] n, and its Theoretical and Physical Properties Studies, Crystal Research and Technology, 2021; 56 (2)120-124. https://doi.org/10.1002/crat.202000124

Mei, L. and Ming, T. H. (2008). Synthesis and Crystal Structure of Mononuclear Bis (2-aminopyridine) zinc Complex, *Asian Journal of Chemistry*, 20(8): 6589-6593.

Morehead, M. S. and Scarbrough, C. (2018). Emergence of global antibiotic resistance". Prim Care, 45(3):467-484.

Okocha, B. I., Orie, K. J., Duru, R. U., & Ngochindo, R. L. (2023). Analysis of the active metabolites of ethanol and ethyl acetate extract of Justicia carnea. *African Journal of Biomedical Research*, 26(1), 109-117.

Orie, K. J., Ngochindo, R. I., and Abayeh, O. J. (2019a). Synthesis of 1, 1-bis (2-carbamoylguanidino) furan-2-ylmethane. *Journal of Chemical Society of Nigeria*, 44(2)163-168

Orie, K. J., Duru, R. U., & Ngochindo, R. I. (2021b). Metal complexes of heterocyclic sulphonamide: synthesis,

characterization and biological activity. Science Journal of Analytical Chemistry, 9(4), 104-109.

Orie, K. J., Duru, R. and Ngochindo, R. I. (2021c). Synthesis and spectroscopic studies of zinc (II) ion and copper (II) ion complexes of 4-methyl-N-(pyridin-2-yl) benzene Sulphonamide", *World Journal of Applied Chemistry*, 6(2):19-24. doi: 10.11648/j.wjac.20210602.12

Ostrowski A. D. and Ford, P. C. (2009). Metal complexes as photochemical nitric oxide precursors: Potential applications in the treatment of tumors", Dalton Transactions, 48,10660-10669. https://doi.org/10.1039/B912898K

Pervaiz, M., Riaz, A., Munir, S., Saeed, Z., Hussain, S., Rashid, A. and Adnan A. (2020) Synthesis and characterization of sulphonamide metal complexes as antimicrobial agents. *Journal of Molecular Structure*, 12 (2): 127284. https://doi.org/10.1016/j.molstruc.2019.127284

Prabhakaran, R., Geetha, A., Thilagavathi, M., Karvembu, R., Krishnan, V., Bertagnolli, H. and Natarajan K, (2004). Synthesis, characterization, EXAFS investigation and antibacterial activities of new ruthenium (III) complexes containing tetradentate Schiffbase. *Journal of inorganic biochemistr*y, 2004; 98(12): 2131-2140. https://doi.org/10.1016/j.jinorgbio.2004.09.020

Rehman, H., Abdul-Qadir, M., Shad, H.A. and Khan, Z.I. (2017). One Pot Synthesis of Some Novel Sulphonamide Derivatives Containing-NH2 Group: Spectral Characterization and Biological Evaluation, Med Chem (Los Angeles), 7: 252-256.

Sani, U., Na'ibi, H. U. and Dailami, S. A. (2017). In vitro antimicrobial and antioxidant studies on N-(2-hydroxylbenzylidene) pyridine-2-amine and its M (II) complexes", *Nigerian Journal of Basic and Applied Sciences*, 25(1):81-88. DOI: 10.4314/njbas.v25i1.11.

Sani, U. and Iliyasu, S. M., (2018). Synthesis, characterization and antimicrobial studies on Schiff base derived from 2-aminopyridine and 2-methoxybenzaldehyde and its cobalt (ii) and nickel (ii) complexes. *Bayero Journal of Pure and Applied Sciences* 2018:11(1):214-219. DOI: 10.4314/bajopas.v11i1.35S

Sultana, N., Naz, A., Arayne, M.S. and Mesaik, M. A. (2010). Synthesis, characterization, antibacterial, antifungal and immunomodulating activities of gatifloxacin–metal complexes, *Journal of Molecular Structure*, 969 (1-3):17-24. htts//doiorg/101016/j.molstru.2010.01.036

Sumrra, S.H., Hassan, A.U., Imran, M., Khalid, M., Mughal, E.U. Nazar, M.F. and Khan, MU, (2020). Synthesis, characterization, and biological screening of metal complexes of novel sulfonamide derivatives: Experimental and theoretical analysis of sulfonamide crystal". *Applied Organometallic Chemistry*, 34(7): 5623, https://doi.org/10.1002/aoc.5623

Tsapkov, V. I., Prisacar, V. I., Buracheva, S.A.. Lazakovich, D. V. and Gulya, A.P. (2008). Synthesis and antimicrobial activity of sulfazine-containing copper (II) coordination compounds with substituted salicylaldehydebenzoylhydrazones, *Pharmaceutical chemistry journal*, 42(9):523-526, https://doi.org/10.1007/s11094-009-0173-7

Vidya, V. G. (2016). Synthesis, Characterization and Biological Studies of a new Cu (II) Complex Derived from 9-Anthraldehyde and 2-Aminopyridine. *Research Journal of Recent Sciences* ISSN, 2277, 2502.2016.

Zahan, M, K. E., Islam, M. S. and Bashar, M. A. (2015). Synthesis, Characterization and antimicrobial activity of Some Metal Complexes of Mn(II), Fe(III) Co(II), Ni(II), Cu(II) and Sb(III) containing bidentate Schiff base of SMDTC, Russian *Journal of general chemistry*, 85:667-672.

Zhang, X., Adedoyin, O., Bertoli, M. L. M., Govor, E. V. and Kavallieratos, M. (2020). Sulphonamide ligand frameworks for Sm (III) extraction from alkaline high-level waste. RAD Conference Proceedings,4, 173–178. DOI: 10.21175/RadProc.2020.35.