

**BEHAVIOUR OF *N*-(2-HYDROXYBENZYLIDENE)PYRAZINE-2-CARBOXAMIDE IN COMPLEXATION TOWARDS FE(II), CO(II), NI(II) AND CU(II) IONS: SYNTHESIS, SPECTRAL CHARACTERIZATION, MAGNETIC AND ANTIMICROBIAL PROPERTIES**

**Festus Chioma\*and Okocha Ogechi**

Department of Chemistry, Ignatius Ajuru University of Education, Rivers State, Nigeria.

**Corresponding Author:** festchi@yahoo.com

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**ABSTRACT**

The new bidentate Schiff base, *N*-(2-hydroxybenzylidene) pyrazine-2-carboxamide was synthesised from pyrazine-2-carboxamide and 2-hydroxybenzaldehyde in alcoholic media. The Schiff base was reacted with FeSO<sub>4</sub>·7H<sub>2</sub>O, Co(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O, Ni(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O, Cu(NO<sub>3</sub>)<sub>2</sub>·3H<sub>2</sub>O to give the corresponding complexes of Fe(II), Co(II), Ni(II) and Cu(II). The synthesised ligand and its metal(II) complexes were characterised by melting point, FTIR, Uv-vis, molar conductance and magnetic susceptibility measurements. The observed shifts in FTIR spectral bands of the complexes with regards to the metal free ligand corroborates coordination of the Schiffbase with the metal ions through the phenolic oxygen and imine nitrogen atoms. The low values of molar conductivity in dimethylsulphoxide (DMSO) confirmed the non-electrolytic nature of the complexes, while the proposed molecular formulas of [M(L)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>]*n*H<sub>2</sub>O and [M(L)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>], indicative of six coordinate octahedral geometry for Fe(II) and Ni(II) complexes; and four coordinate tetrahedral/square planar geometries for Co(II) and Cu(II) were consistent with the data of the elemental, spectral, magnetic and percentage metal analyses. Also, analytical and spectral results confirmed 2L:1M stoichiometry for the complexes. The synthesised compounds were evaluated for antimicrobial activities and found to be active against the bacteria and fungi organisms.

**Keywords:** Antimicrobial agents, pyrazine-2-carboxamide, bidentate Schiff base, octahedral

**INTRODUCTION**

The world major health challenge has remained the rapid resistance development possessed by infectious diseases to already known antibiotics. This has led to annual loss of lives [1]. As the days go by, microorganisms develop specialized means of resistance to current antibiotics; i.e. extrusion of antibiotics (efflux bomb) preventing their accumulation in the bacteria cells which in-turn inhibits the action of antibiotic agents [2]. Due to the rise in multidrug resistance by pathogenic microbes, antibiotic toxicities and lack of selectiveness, the need to design, syntheses and evaluate novel antibiotic compounds or derivatives of current antibiotics with low metal ion toxicity, broad spectrum activity, enhanced mechanism of microbial resistance, improved selectivity and with a new reaction mechanism unknown to the microbes [3] is highly significant. Metal ions and their

derivatives have been applied as diagnostic, pharmacological and antibiotic agents in the treatment of various infectious diseases. Metal ions in various oxidation states, over the decades have drawn considerable research attention due to their significant roles in the effective functioning of living organisms. These metal ions at trace and ultra-trace quantities interact with organic molecules in biological systems [4] faster to exact vital functions at the molecular levels, a consequence of their (i) nuclei size, (ii) electron availability with which they bind to biomolecules, (iii) ability to prevent premature aging and cell breakdown and (iv) ability to act as catalysts to trigger both enzymatic reactions and vitamins' functions in bodily systems [5]. Furthermore, metal ions, in enzyme-catalytic processes form enzyme active sites and stabilize tertiary/quaternary structures of enzymes. Enzymatic activities are completely dependent on metal ions, for example, the human system requires  $\pm 2$  g of zinc daily to support the functionality of  $\pm 100$  enzymes, while 4-5 mg of copper are needed for the repair of calcium in the bones and connective tissues [6,7]. Additionally, oxidation of amines and ascorbic acid, oxygen distribution in invertebrates, photosynthesis in green plants and production of neurotransmitters, epinephrine and norepinephrine in the nervous system are all triggered in the presence of copper [8]. Ribonucleotide reductase and glutamic mutase enzymes involved in the biosynthesis of DNA and metabolism of amino acids functions in the presence of cobalt. Cobalt as a major component of vitamin B<sub>12</sub>, acts as a coenzyme and serves as a prosthetic group that is tightly bound to many enzymes in the body. Similarly, manganese which is significant in the oxygen evolution process of photosynthesis also acts as a co-factor to pyruvate carboxylase enzyme in conversion of non-carbohydrate substances into glucose in the body, while iron which constitutes about 0.35% of the entire haemoglobin is an essential element that stimulates oxygen distributions in the body (from lungs to the cells), aids in oxygen storage in the muscle tissue, facilitates electron distribution in plants and animals and increases the functions of enzymes such as nitrogenase, succinic dehydrogenase, etc.

Generally, metal ions bind favourably to organic molecules forming stable metal-organic compounds of greater therapeutic uses [9-11]. But certain metallo elements (Fe, Co, Cu and Zn) at trace levels have been reported for decades to accelerate the efficacy of metal-organic compounds when administered as therapeutic and toxicological agents. The choice of metal ions in metal-organic drug/compound designs, isolation and evaluation depends on their oxidation state; involvement in regulation of physiological processes; charge; nature, structure and size of the metal-organic compounds to be formed; and the biological importance of the metal ions [12]. The plan and synthesis of divalent metal complexes with enhanced therapeutic applications but little or no toxic side-effects has been concern. So, this study is targeted at the synthesis and spectral characterization of metal (II) complexes (where Metal (II) = Fe, Co, Ni and Cu) involving synthesized Schiff base, *N*-(2-hydroxybenzylidene) pyrazine-2-carboxamide. The metal (II) complexes will be assessed for different magnetic behaviours/interactions. Lastly, the effectiveness of the Schiff base and its metal (II) complexes as antimicrobial agents will be examined.

## **MATERIALS AND METHODS**

### **Experimental**

Reagent grade pyrazine-2-carboxamide and 2-hydroxy-benzaldehyde were purchased from Sigma Aldrich. Iron(II) sulphate heptahydrate, cobalt(II) nitrate hexahydrate, nickel(II) nitrate hexahydrate and copper(II) nitrate dehydrate, glacial acid, triethylamine, dimethyl sulphoxide, ethanol and anhydrous calcium chloride were all obtained from BDH and Merck chemicals. All the chemical

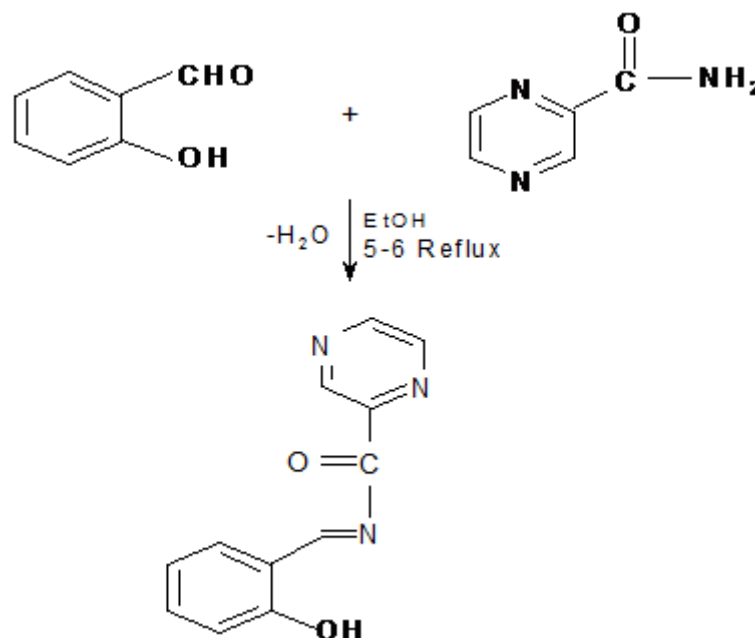
reagents and solvents were used as received without further purifications. At the range 190–900 nm, the electronic (UV/Vis) spectra of the compounds in DMSO were recorded using Perkin Elmer  $\lambda$ 25 spectrophotometer. Microanalyses (CHN) were determined on an Elementar, Vario EL Cube setup. Perkin Elmer FT-IR spectrum BX spectrophotometer was used to record the infrared spectra of the bidendate Schiff base, HL and its divalent metal-based compounds as KBr pellets at the range of 4000–350  $\text{cm}^{-1}$ . Molar conductivity measurements in DMSO ( $1 \times 10^{-3}$  M) at 28°C were obtained on a Systronics 611 conductivity bridge. The Schiff base and its divalent metal-based compounds were evaluated for melting points using in open glass capillary tubes on Electro-thermal Temp-Mel melting point apparatus. Magnetic susceptibilities were measured on a Sherwood susceptibility balance MSB Mark 1 at a temperature of 303K. The diamagnetic corrections were calculated using Pascal's constant [13] from the equation.

$$\mu_{\text{eff.}} = 2.828\sqrt{\chi T}$$

## Synthesis

### Synthesis of *N*-(2-hydroxybenzylidene) pyrazine-2-carboxamide; HL

Equimolar mixture of pyrazine-2-carboxamide (0.0172mol, 2.099g) and 2-hydroxybenzaldehyde (0.0172mol, 3.00g) with a catalytic amount of glacial acetic acid (1.5-2.0 mL) in ethanol (45 mL) was refluxed for 5h on a magnetic stirrer hot plate. The yellow shade solid product *N*-(2-hydroxybenzylidene)pyrazine-2-carboxamide obtained on cooling in ice (302 K), was filtered, washed with little ethanol and dried over anhydrous calcium chloride. Yield (78.5%); colour (yellow); melting point(213-215°C);CHN (%)-Anal (Calcd): C, 57.96 (58.14), H, 3.97 (3.99), N, 18.70 (18.51);IR ( $\text{cm}^{-1}$ ):  $\nu_{\text{OH}}$ (3415<sub>s</sub>),  $\nu_{\text{C=N}}$ (1715<sub>s</sub>),  $\nu_{\text{C=C}}$ (1610<sub>s</sub>),  $\nu_{\text{C-O}}$ (1160<sub>s</sub>); UV( $\text{cm}^{-1}$ ): 28605 ( $n-\pi^*$ ) 37.60, 31551 ( $\pi-\pi^*$ ). Formula mass: 227.222 g/mol.



**Figure 1: Synthesis of Schiff base Ligand, HL**

### Synthesis of divalent metal-based compounds

Applying slight modifications, the divalent metal-based complexes were synthesized by the literature method [14]. To a hot solution (15 mL; 60°C) of *N*-(2-hydroxybenzylidene)pyrazine-2-carboxamide (0.2g,  $4.4 \times 10^{-4}$  mol) in ethanol, 0.103-0.129 g (0.00044 mol) of each metal salt

[M(NO<sub>3</sub>)<sub>2</sub>.nH<sub>2</sub>O (Co, Ni, n=6 and Cu n=2) and M(SO<sub>4</sub>)<sub>2</sub>.nH<sub>2</sub>O (Fe, n=7)] pre-dissolved in hot ethanolic solution (10 mL; 60°C) was added. The reaction mixture was in each case buffered with 3 mL of (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>N to raise and maintain a pH of 8-9 and then refluxed on magnetic-stirrer hot plate for about 6 h with continuous stirring. The solid complexes formed were collected by filtration, recrystallized with EtOH and dried over anhydrous calcium chloride in a desiccator.

[Fe(C<sub>24</sub>H<sub>20</sub>N<sub>6</sub>O<sub>6</sub>)]Yield (87.50%); colour (chocolate solid, a shade of brown); melting point(274-276°C); CHN (%) -Anal (Calcd): C, 53.01 (52.95), H, 4.18 (3.90), N, 15.57, (15.45); IR(cm<sup>-1</sup>): νC=N(1685<sub>s</sub>), νC=C(1568<sub>s</sub>), νC-O(1120<sub>s</sub>), νM-N(542<sub>s</sub>), M-O(433<sub>s</sub>); UV (cm<sup>-1</sup>): 44905 cm<sup>-1</sup>, 40310 cm<sup>-1</sup>(C.T), 37530 cm<sup>-1</sup>(π→π\*), 20161 cm<sup>-1</sup>(<sup>5</sup>T<sub>2g</sub>→<sup>5</sup>B<sub>1g</sub>), 16528 cm<sup>-1</sup>(<sup>5</sup>T<sub>2g</sub>→<sup>5</sup>A<sub>1g</sub>). Formula mass: 544.314; %metal(cal.) 10.51(10.26); μ<sub>eff</sub>(5.08 B.M.); molar conductance (ohm<sup>-1</sup>mol<sup>-1</sup>cm): 5.40.

[Co(C<sub>24</sub>H<sub>16</sub>N<sub>6</sub>O<sub>4</sub>)]·2H<sub>2</sub>OYield (79.55%); colour(gold, a shade of yellow); melting point(289-291°C);CHN (%) -Anal (Calcd): C, 52.71 (52.66), H, 3.83 (3.68), N, 15.44, (15.37); IR(cm<sup>-1</sup>): νOH(3436<sub>s</sub>), νC=N(1644<sub>s</sub>), νC=C(1587<sub>m</sub>), νC-O(1170<sub>s</sub>), νM-N(510<sub>s</sub>), M-O(480<sub>s</sub>); UV (cm<sup>-1</sup>): 44052 cm<sup>-1</sup>(C.T), 32848 cm<sup>-1</sup>(π→π\*), 27049 cm<sup>-1</sup>(n→π), 19165 cm<sup>-1</sup>(<sup>4</sup>A<sub>2</sub>→<sup>4</sup>T<sub>1</sub>), 14684 cm<sup>-1</sup>(<sup>4</sup>A<sub>2</sub>→<sup>4</sup>T<sub>1</sub>(P), 12165 cm<sup>-1</sup>: Formula mass 547.394; %metal(cal.) 10.50(10.76); μ<sub>eff</sub>(4.17B.M.); molar conductance (ohm<sup>-1</sup>mol<sup>-1</sup>cm): 12.14. and

[Ni(C<sub>24</sub>H<sub>20</sub>N<sub>6</sub>O<sub>6</sub>)]Yield (87.50%); colour(ruby, a shade of red); melting point(274-276°C);CHN (%) -Anal (Calcd): C, 52.72 (52.68), H, 3.77 (3.68), N, 15.53 (15.37); IR(cm<sup>-1</sup>): νOH(3400<sub>m</sub>), νC=N(1659<sub>s</sub>),νC=C(1592<sub>s</sub>), νC-O(1167<sub>s</sub>), νM-N(508<sub>s</sub>), M-O(483<sub>s</sub>); UV (cm<sup>-1</sup>): 45455 cm<sup>-1</sup>(C.T), 30303-37175 cm<sup>-1</sup>(π→π\*), 26246-29412 cm<sup>-1</sup>(n→π), 23256 cm<sup>-1</sup>(<sup>3</sup>A<sub>2g</sub>→<sup>3</sup>T<sub>1g</sub>(P)), 14045-17921 cm<sup>-1</sup>(<sup>3</sup>A<sub>2g</sub>→<sup>3</sup>T<sub>1g</sub>), 11416-12569 cm<sup>-1</sup>(<sup>3</sup>A<sub>2g</sub>→<sup>3</sup>T<sub>2g</sub>). Formula mass: 547.174; %metal(cal.) 10.42(10.72); μ<sub>eff</sub>(2.00 B.M.); molar conductance (ohm<sup>-1</sup>mol<sup>-1</sup>cm): 6.54.

[Cu(C<sub>24</sub>H<sub>16</sub>N<sub>6</sub>O<sub>4</sub>)]·H<sub>2</sub>O Yield (89.28%); colour (lime, a shade of green); melting point(267-269 °C);CHN (%) -Anal (Calcd): C, 54.81 (53.78), H, 3.46 (3.39), N, 16.77 (15.69); IR(cm<sup>-1</sup>): νOH(3417<sub>b</sub>), νC=N(1659<sub>s</sub>), νC=C(1586<sub>s</sub>), νC-O(1164<sub>s</sub>), νM-N(572<sub>s</sub>), M-O(495<sub>s</sub>); UV(cm<sup>-1</sup>): 42373 cm<sup>-1</sup>(C.T), 37037, 30303 cm<sup>-1</sup> (π→π\*), 28490, 26246 cm<sup>-1</sup>(n→π\*), 14859, 12610 cm<sup>-1</sup>(<sup>2</sup>T<sub>2g</sub>→<sup>2</sup>E<sub>g</sub>). Formula mass: 536.004; %metal(cal.) 11.24(11.53); μ<sub>eff</sub>(2.20 B.M.); molar conductance (ohm<sup>-1</sup>mol<sup>-1</sup>cm): 9.01.

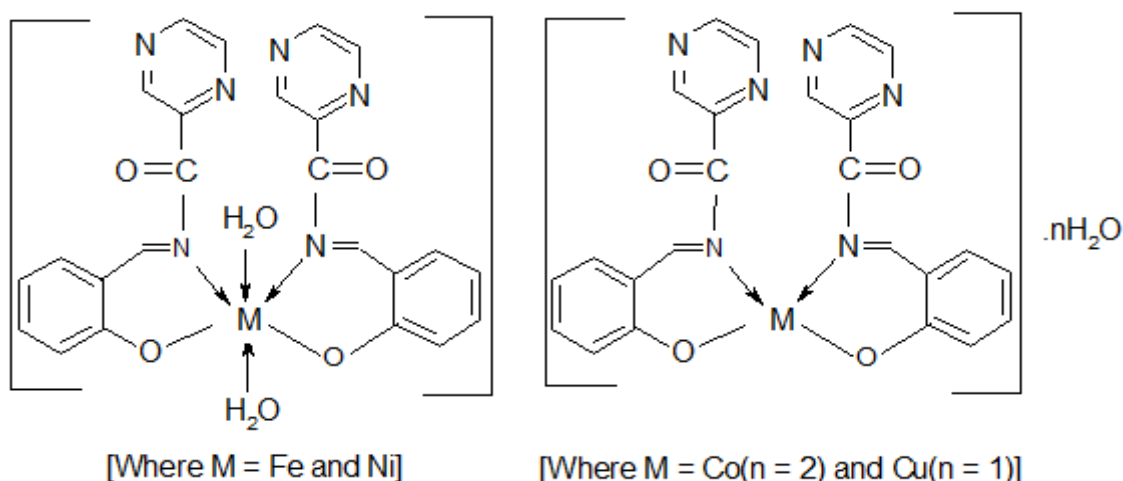


Figure 2: Proposed Structures for the Metal-Based Compounds

## BIOLOGICAL STUDIES

### ANTIMICROBIAL ASSAYS

The biological activities of the bidendate Schiff base, HL and its divalent metal-based complexes were evaluated for their antibacterial and antifungal activities using Agar and Disc diffusions' techniques respectively. The in-vitro antibacterial activities of the synthesized compounds were screened against *E. coli*, *S. aureus*, *B.cereus*, *P. mirabilis*, *P. aeruginosa*, and *K. oxytoca*. The in-vitro antifungal activities were determined against *Aspergillus niger*, *Aspergillus flevus* and *R. Stolonifer*.

#### Antibacterial Studies

About 38 g of pure dehydrated Muller-Hinton agar media was dissolved in 1000 mL of distilled water and used for the antibacterial screening. The bacterial strains *E. coli*, *S. aureus*, *B. cereus*, *P. mirabilis*, *P. aeruginosa*, and *K. oxytoca*, obtained in their pure culture states by inoculating in the nutrient broth, were incubated at 37-39 °C for about 18-20 h and used. The above Muller-Hinton agar media was used to prepare the petri dishes on which 6 mm wells were bored with sterile metallic cork borer (6 mm). 0.3 mL of 18-20 h test bacteria cultures were uniformly inoculated on the surface of the Muller Hinton's agar in petri dish. 0.06 mL of the 10 mg/mL solution of each complex prepared in DMSO was poured into 6mm wells bored on the agar using a micropipette and uniformly spread using bent glass rod. The plates were allowed to stand on the bench for 45min before incubation at 35°C for 48 h after which inhibition zone growth in diameter (mm) was measured as antibacterial activity. All antibacterial activities were calculated as mean of three replicates. The drug streptomycin was used as standard.

#### Antifungal Studies

A disc technique was employed *in vitro* to determine the antifungal activities of the synthesized compounds. Unpeeled but washed-sliced potatoes (250 g), dextrose (25 g), and agar (25 g) in 1250 mL distilled water were used to prepare the 'potato dextrose agar (PDA) media used for the antifungal screening. The antifungal screening (*in vitro*) was carried out against *Aspergillus niger*, *Aspergillus flevus* and *R. Stolonifer*. The pure cultures of *Aspergillus niger*, *Aspergillus flevus* and *R. Stolonifer* were uniformly inoculated on the surface of the PDA solution petri dish. 15µg of the stock solutions of each test sample (1mg/mL) prepared by dissolving 10mg of the synthesized compound in 10mL of dimethyl sulphoxide (DMSO) solvent was poured a 6 mm well bored on the PDA with a 6mm sterile metallic cork borer. All the plates inoculated were incubated at 35°C for 48 h after which inhibition zone growth in diameter (mm) was measured as antifungal activity with antibiogram zone scale. All antifungal activities were determined as mean of three replicates. The drug fluconazole was used as standard.

## RESULTS AND DISCUSSIONS

### Physico-chemical characterizations

The bidendate Schiff base, HL, reacted with the divalent metal salts in 2L:1M molar ratio in alcoholic medium to afford divalent metal-based compounds with various shades and varied melting points, different from their starting materials. The synthesized Schiff base and its divalent metal-based compounds were generally stable at room temperature, non-hygroscopic and soluble in organic solvents i.e. ethanol, methanol, DMF, DMSO and chloroform.

### FTIR Spectroscopy

Infrared spectroscopy studies absorption frequency for vibration of bonds in a molecule. It has been applied to determine if or not imine bond ( $\text{-C=N-}$ ) has been formed in Schiff bases and whether or not there is a shift in the  $\text{-C=N-}$  absorption band(s) of their metal complexes. The HL ligand spectrum displayed a broad band at  $3415\text{ cm}^{-1}$  consistent of  $\nu(\text{OH})$  stretching vibration which disappeared in all the divalent metal-based compounds, indicative of H-atom removal, followed by metal-oxygen bond formation. The bands exhibited between  $3400\text{--}3436\text{ cm}^{-1}$  in all the metal-based compounds exception of Fe(II) complex were assigned to  $\nu(\text{OH})$  of coordinated water molecules. A sharp lone band observed at  $1715\text{ cm}^{-1}$  in the spectrum of the ligand is assigned to uncoordinated  $\text{C=N}$  stretching vibration. The band still remained single and strong but suffered low shifts at  $1685\text{--}1644\text{ cm}^{-1}$  range in all metal-based compounds, thus confirming the involvement of the imine N atom in coordination to divalent metal ions. Consequently, the appearance of the  $\nu\text{C=N}$  band in the metal-based compounds as single strong band indicate cis-isomeric form of geometric isomerism (Figure 2). Cis-isomeric metal-based compounds have been reported to exhibit single  $\nu\text{C=N}$  bands while those in trans-isomeric form display double  $\nu\text{C=N}$  bands [14,17]. The observed variation in the stretching vibration of  $\delta\text{C-H}$  in the metal-based compounds ( $\pm 35\text{ cm}^{-1}$ ) from that of the ligand ( $1023\text{ cm}^{-1}$ ) is attributed to the pseudo-aromatic nature of the chelates [18]. The bands at  $508\text{--}572\text{ cm}^{-1}$  and  $433\text{--}495\text{ cm}^{-1}$  ranges which were not observed in the bidentate Schiff base spectrum were assigned to  $\nu\text{M-N}$  and  $\nu\text{M-O}$  stretching vibrations of the metal complexes [19,20].

### Electronic spectra and magnetic moment

The ultraviolet spectra of the Schiff base and its divalent metal-based compounds were characterized by transition bands within the Schiff base i.e.  $n\text{-}\pi^*$  ( $26247\text{--}29155\text{ cm}^{-1}$ ) and  $\pi\text{-}\pi^*$  ( $30303\text{--}37594\text{ cm}^{-1}$ ) and charge transfer (metal-to-Schiff base and Schiff base-to-metal) transitions ( $42373\text{--}48077\text{ cm}^{-1}$ ) respectively with molar absorptivity of  $10\text{--}46\text{ M}^{-1}\text{ cm}^{-1}$ .

The electronic spectrum of the divalent iron-based compound showed two  $d\text{-}d$  bands at  $16250\text{ cm}^{-1}$  and  $20120\text{ cm}^{-1}$  attributed to  ${}^5\text{T}_{2g}\rightarrow{}^5\text{A}_{1g}$ , and  ${}^5\text{T}_{2g}\rightarrow{}^5\text{B}_{1g}$  transitions, of a high spin  $d^6$  octahedral geometry [21]. The appearance of doublet band in the spectrum of the divalent iron-based compound was assigned to Jahn-Teller distortion in the excited state [22]. The observed magnetic moment of 5.08 B.M corroborated the assignment of a high spin octahedral geometry to the iron-based compound [23].

The electronic spectra of the synthesised divalent cobalt-based compounds exhibited two absorption bands both at the ultraviolet and visible regions at  $32848$  and  $27049\text{ cm}^{-1}$ ; and  $19165$  and  $14684\text{ cm}^{-1}$ . The bands at  $32848$  and  $27049\text{ cm}^{-1}$  were typical of  $\pi^*\leftarrow\pi$  and  $\pi^*\leftarrow n$  transitions while the bands around  $19165$  and  $14684\text{ cm}^{-1}$  were consistent of tetrahedral geometry with  ${}^4\text{A}_2\rightarrow{}^4\text{T}_1(\nu_2)$  and  ${}^4\text{A}_2\rightarrow{}^4\text{T}_1(\text{P})(\nu_3)$  transitions respectively [24]. The latter were consistent of the electronic configuration of  $e^4t^3$  (high spin). The transition band around  $5000\text{--}6000\text{ cm}^{-1}$  frequently linked to  ${}^4\text{A}_2\rightarrow{}^4\text{T}_2$  transition in the four coordinate divalent cobalt-based compounds was not observed, since it tailed into the infrared region, [25]. The observed magnetic moment of 4.17 B.M was suggestive of high spin tetrahedral geometry to the divalent cobalt-based compound studied since  $\mu_{\text{eff}}$  of divalent cobalt-based complexes are expected to exhibit higher spin-only values due to orbital contributions [26].

Divalent nickel-based compounds usually undergo several structural switches from four-coordinate square planar to tetrahedral or/and to six-coordinate octahedral geometry [27]. The electronic spectra of divalent nickel complexes are also characterized by different complicated equilibria [28]. The

observance of three absorption bands at 11416-12576  $\text{cm}^{-1}$ , 14880-17921  $\text{cm}^{-1}$  and 23640  $\text{cm}^{-1}$  was indicative of octahedral geometry and is assigned to ( ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{2g}$ ), ( ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}$ ) and ( ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{P})$ ) transitions [29]. A magnetic moment of 2.00 B.M was complimentary of octahedral geometry  $d^8$  nickel-based compound.

$d^9$  copper-based compounds in cubic environments are susceptible to Jahn Teller distortions giving rise to unsymmetrical or multiple bands. Divalent copper complexes with a  $t_{2g}^6 e_g^3$  configuration and ground term of  ${}^2\text{D}$  often display single absorption band typical of  ${}^2\text{E}_g \rightarrow {}^2\text{T}_{2g}$  transition in the octahedral field. However, six coordinate divalent copper complexes are often susceptible to Jahn Teller distortions, a consequence of uneven distribution of electrons in the  $e_g$  set of the  $3d$  orbitals [30] resulting to tetragonally distorted octahedral geometry [31]. Square planar divalent copper complexes displays bands around 13000-20000  $\text{cm}^{-1}$  region, while regular tetrahedral divalent copper complexes exhibits single absorption band below 10000  $\text{cm}^{-1}$  [32]. The synthesized divalent copper-based compound displayed two asymmetric bands at 14858  $\text{cm}^{-1}$  and 18050  $\text{cm}^{-1}$  assigned to  ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$  and  ${}^2\text{B}_{1g} \rightarrow {}^2\text{E}_{1g}$  transitions in a square planar environment [33]. A moment of 1.9-2.2 B.M. is usually observed for mononuclear divalent copper complexes [34,35]. The divalent copper-based compound had a magnetic moment of 2.20 B.M. and was consequently mononuclear [36]. The ultraviolet spectra of the synthesised divalent copper-based compound displayed three absorptions at the ranges 262460-28490  $\text{cm}^{-1}$ , 30303-37037  $\text{cm}^{-1}$  and 42373  $\text{cm}^{-1}$  consistent of  $\pi^* \leftarrow n$ ,  $\pi^* \leftarrow \pi$  and charge transfer transitions.

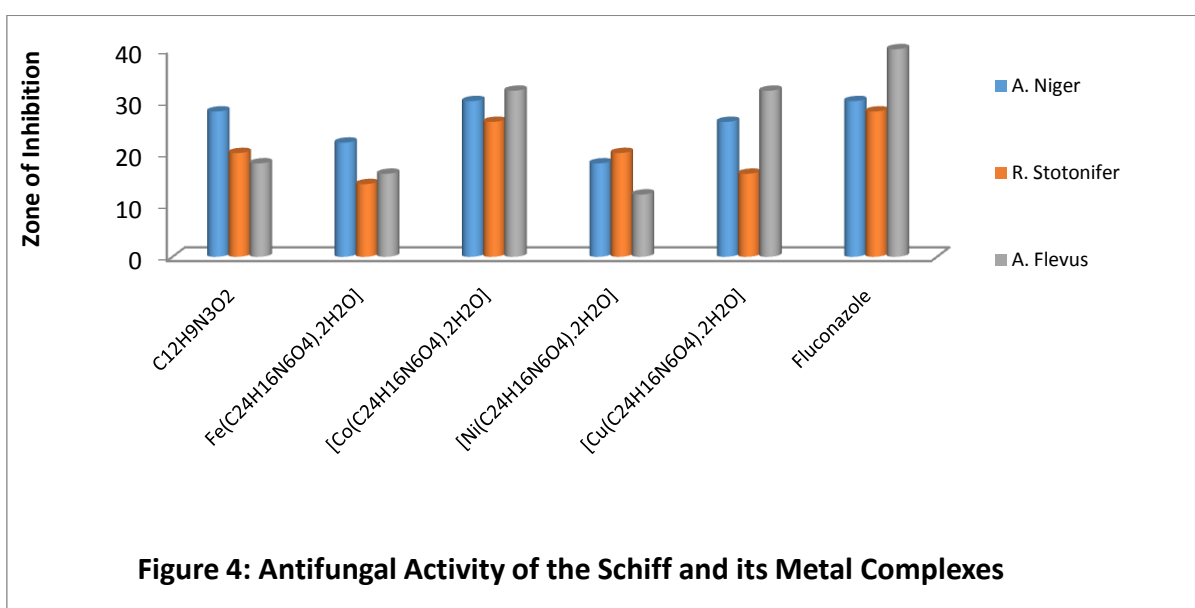
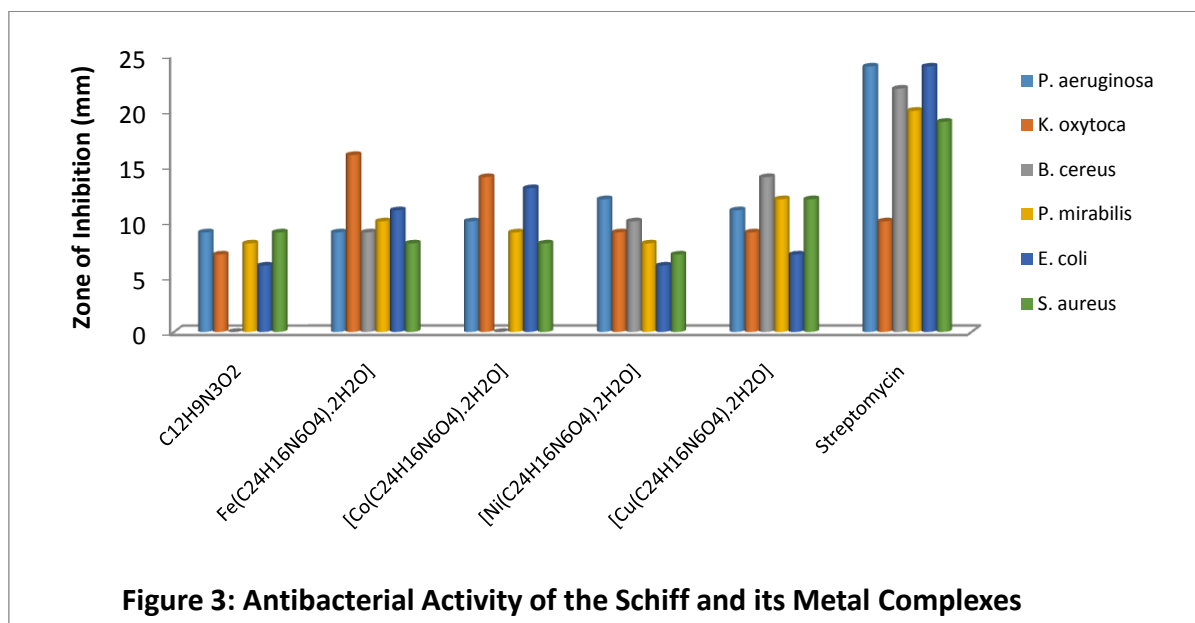
### Elemental, Conductance and Quantitative Measurements

The composition and molecular formula of the ligand and its divalent metal-based compounds were assigned on the basis of elemental analysis. The elemental data of the synthesised metal-based compounds were in good agreement with the calculated (theoretical) values and conformed to proposed structures. Similarly, the elemental analysis showed that the metal ions reacted with the Schiff base in 1:2 molar ratio for the divalent metal-based compounds. The synthesized divalent iron, cobalt, nickel and copper based compounds were non-electrolytes in dimethylsulphoxide ( $1 \times 10^{-3}$ ). Their molar conductance values of 5.40, 12.14, 6.54 and 9.01  $\text{ohm}^{-1} \text{mol}^{-1} \text{cm}$  were lower than reported values of 45.0-70.0  $\text{ohm}^{-1} \text{mol}^{-1} \text{cm}^2$  and 90.0-120  $\text{ohm}^{-1} \text{mol}^{-1} \text{cm}^2$  for a 1:1 and 1.2 electrolytes respectively. The molar conductivity values were corroborated by quantitative analysis carried out with divalent iron sulphate solution and nitric acid which displayed no brown-ring layer/precipitate indicating absence of nitrate and corroborating the complexes as neutral.

### Antimicrobial Studies

The *in vitro* antimicrobial activity of the bidentate Schiff base, HL, and its divalent metal-based compounds were screened against bacterial strains (*E. coli*, *S. aureus*, *B. cereus*, *P. mirabilis*, *P. aeruginosa*, and *K. oxytoca*) and fungal strains (*Aspergillus niger*, *Aspergillus flavus* and *R. Stonifer*) by Agar and Disc diffusions' methods. Using the inhibition zone growth diameter as criteria for measurement, the activities of the synthesized compounds against the bacterial and fungal strains with some known antibiotics (streptomycin and fluconazole) were determined and are presented in figures 3 and 4. A critical examination of the figures reveals that the divalent metal-based compounds exhibited promising results in one way or the other than the Schiff base against tested microorganisms. The enhanced activity of the metal-based compounds is explained on the basis of Chelation theory (Mittal and Uma, 2010), the presence of azomethine moiety and hetero atoms in their structures.  $[\text{Fe}(\text{C}_{24}\text{H}_{16}\text{N}_6\text{O}_4)(\text{H}_2\text{O})_2]$  and  $[\text{Co}(\text{C}_{24}\text{H}_{16}\text{N}_6\text{O}_4)].2\text{H}_2\text{O}$  were more potent

against the tested *K. oxytoca* than the standard drug, streptomycin, while the antifungal activity of  $[F(C_{24}H_{16}N_6O_4)(H_2O)_2]$  was comparable to that fluconazole against *Aspergillus niger*. The less biocidal activity displayed by the Schiff base could be due to the production of potent protein toxins which activate the bacteria cell surface proteins and in turn prevents its adequate permeation into the bacteria cells [37].



## CONCLUSION

New Fe(II) Co(II) Ni(II) and Cu(II) complexes of *N*-(2-hydroxybenzylidene)pyrazine-2-carboxamide were synthesized and characterized. Percentage metal, electronic, magnetic susceptibility, and molar conductance measurements of the complexes show that divalent iron and nickel complexes assumed octahedral geometry while tetrahedral/square planar geometries were adopted by Co(II) and Cu(II) complexes. Generally, the complexes were non-electrolytic and mononuclear in nature. The *in-vitro* antimicrobial investigations revealed that the Schiff base and its divalent metal complexes displayed moderate to good antibacterial/antifungal properties.



### Conflict of Interests

The authors declare that there is no conflict of interests with respect to the publication of this research paper.

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