



# Synthesis, Characterization and *in silico* Molecular Docking studies of Cr, Co and Fe (III) Metal Complexes with *Mycobacterium* Tuberculosis Enzyme glutamine Synthetase (GS) a Schiff base ligand Derived from 2-hydroxy-1-naphthaldehyde

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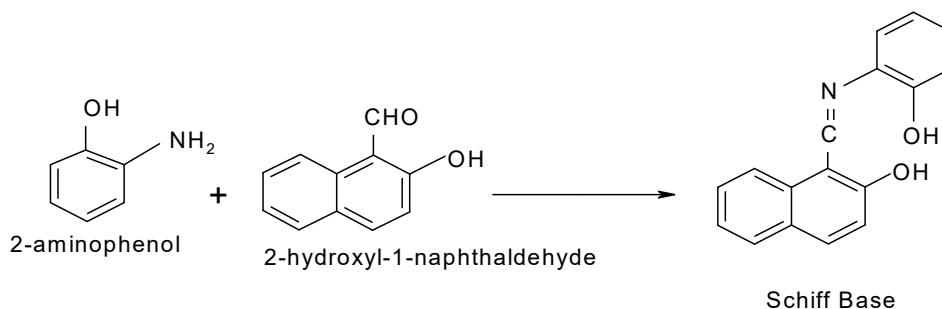
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**Abstract:** The complexes of Ru(III) derived from 2-hydroxyl-1-naphthaldehyde ligands, (HL1 and HL2), were synthesized and characterized using <sup>1</sup>H NMR, <sup>13</sup>C{H}NMR, FT-IR, UV-Vis, elemental (CHN)/metal content analysis, TGA/DSC, PXRD, Magnetic susceptibility and Conductivity measurements. The IR spectral data showed that the ligands acted as bidentate ligands coordinated to the Cr, Co, and Fe(III) ion through phenolic oxygen atom of the hydroxyl group (O-H), and the nitrogen atom of the azomethine (HC=N), whereas the bond that occurred via oxygen atom of the water molecule completed the geometry.

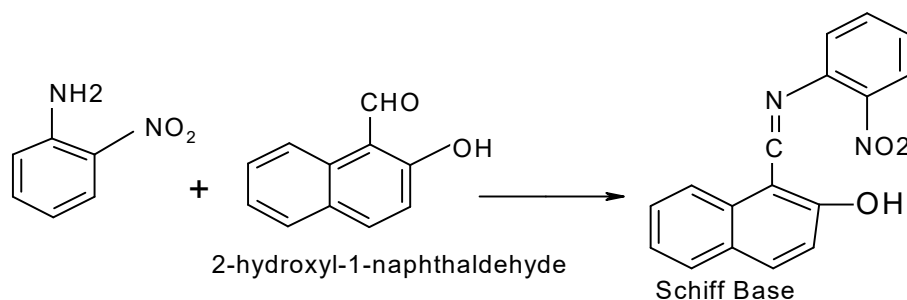
**Keywords:** 2-nitroaniline, 2-aminophenol, Metal complexes, 2-hydroxyl-1-naphthaldehyde, Schiff bases, Chromium, Cobalt and iron (III) metals.

## INTRODUCTION

Schiff bases have gained recognition as one of the frontline ligands in the field of coordination chemistry due to their stability, flexibility toward coordination, ease of synthesis and structural diversity. These ligands are good chelating agents toward transition and main group metals (Abbas and Refat, *et al.*, 2016). In recent time, Schiff bases derived from amines with aldehydes or ketones (from 2-hydroxyl-1-naphthaldehyde) are gaining more attention due to their versatility (Ayyavoo *et al.*, 2021 and (Fugu, *et al.*, 2013). Schiff base of 2-nitroaniline and 2-amino phenol, are class of compounds containing RC=NH group and they are obtained via condensation of amines with aldehydes or ketones (Lv, *et al.* and Naureen, *et al.*, 2021).



**Scheme 1:** Schiff base derived from 2-aminophenol and 2-hydroxynaphthaldehyde



**Scheme 2:** Schiff base derived from 2-nitroaniline and 2-hydroxynaphthaldehyde

Schemes shows the Schiff base derived from (a) 2-aminophenol and 2-hydroxy-1-naphthaldehyde and (b). 2-nitroaniline with 2-hydroxy-1-naphthaldehyde and this gave them ability to coordinate to metals in 1:1. The chemistry of these compounds, especially those containing oxygen and nitrogen donor atom together with their metal complexes are receiving attention owing to their fascinating biological activities (Daravath, *et al.*, and Savcı, *et al.*, 2021). Chemotherapeutic ability of Ruthenium complexes and its derivatives in the management of various diseases is well known (Bonnett, *et al.*, 2018 and de Faria, *et al.*, 2021). The Schiff base ligands reported here in these research work were synthesized via condensation of 2-aminophenol and 2-nitroaniline with 2-hydroxy-1-naphthaldehyde in methanol as solvent at room temperature.

## MATERIALS AND METHODS

All chemicals and solvents were grade and used as received. These reagents were used without any purification. They include: 2-hydroxy-1-naphthaldehyde, 2-nitroaniline, ruthenium chloride hexahydrate, methanol, ethanol, diethyl ether, ethyl acetate, chloroform, dichloromethane, hexane, dimethyl sulfoxide, dimethylformamide, acetone and tetrahydrofuran.

### procedure for the Synthesis of the ligands (HL1 and HL2)

The Schiff base ligands HL1 and HL2 were synthesized according to modified literature procedures (Fugu, *et al.*, 2013). 2-hydroxy-1-naphthaldehyde (5 mmol, 0.86 g) was weighed and dissolved in 20 ml of ethanol. The ethanolic solution was mixed with each of the selected amines: 2-aminophenol (5 mmol, 0.545 g) and 2-nitroaniline (5 mmol, 0.691g), in 20 ml of methanol respectively, followed by the addition of 3 drops of conc. H<sub>2</sub>SO<sub>4</sub>. The mixture was

refluxed for about 3-4 hours at room temperature. The product obtained was washed with diethyl ether. Followed by drying in a desiccator over fused calcium chloride ( $\text{CaCl}_2$ ). This gave the Schiff base ligands: HL1-HL2.

#### **General procedure for the synthesis of the metal complexes**

The complexes were prepared using 1:1 mole ratio of metal to ligand following a standard procedure (Fugu, *et al.*, 2013 and Naureen, *et al.*, 2021).  $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$  (1 mmol, 0.266 g, 1 eq),  $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$  (1 mmol, 0.198 g, 1 eq), and  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  (1 mmol, 0.258 g, 1 eq), was weighed and dissolved in 20 ml of methanol and mixed with 20 ml methanolic solution of HL1 and HL2. The mixture was refluxed for about 3 hours using a hot plate magnetic stirrer. The product obtained was filtered and washed with an appropriate solvent and dried over fused  $\text{CaCl}_2$  in a desiccator.

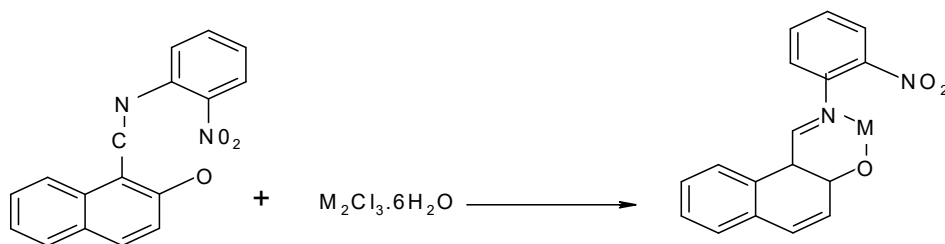
#### **Measurements**

The synthesized compounds were subjected to physical and spectroscopic analyses to confirm their formation. These include  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, FTIR, UV-Visible, Elemental-CHN analysis, TGA/DSC, Powdered x-ray diffraction and Metal analysis. The  $^1\text{H}$  and  $^{13}\text{C}\{\text{H}\}$  NMR spectra were recorded on Bruker 500 MHz and 125 MHz, respectively. The Infrared spectral data were obtained using Tensor 27 Bruker and Perking Elmer FT-IR spectrometer BX. The elemental content (CHN) of the ligand and their complexes was obtained using VarioElementar III microbe CHN analyser. All NMR, and the Magnetic susceptibility values analyses were conducted at room temperature, and the chemical shifts are reported in parts per million (ppm) relative to tetra methylsilane which is used as internal standards for  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR in  $\text{DMSO-d}_6$ .

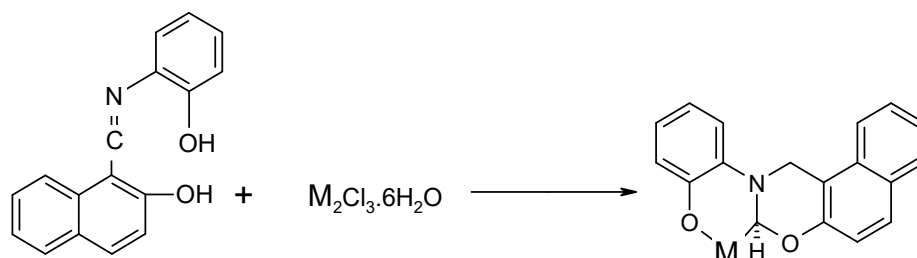
#### **RESULTS AND DISCUSSION**

The Schiff base ligands HL1 and HL2 were synthesized via condensation of 2-aminophenol and 2-nitroaniline with 2-hydroxyl-1-naphthaldehyde in 1:1 mole ratio of amine to aldehyde, using methanol as a solvent.

The Schiff bases were obtained as yellow and red powdered solids respectively, they are air and moisture stable, soluble in polar solvents but insoluble in non-polar solvents. However, the intensity of the colors varies and could be due to the influence of the chromophore groups in the Schiff base ligands. The metal complexes were obtained by the reaction of the Schiff bases with Chromium, Cobalt and Iron (III) metal salt in 1:1 mole ratio at a room temperature. The complexes were obtained in moderate yield as coloured shiny solids; there was variation of color intensity observed on the complexes. They are soluble in methanol, ethanol, dimethyl Sulphur oxide (DMSO), dimethyl fluoride (DMF) and water, but insoluble in non-polar solvents such as chloroform, dichloromethane and N-hexane. The solubility of the ligands and their complexes in polar solvents suggested that they probably polar compounds. The molar conductivity measurement of solution of the complexes in (methanol,  $10^{-3}\text{M}$ ) was found between the range of  $17 \times 10^{-3}$  and  $6 \times 10^{-3} \text{ Scm}^2 \text{ mol}^{-1}$ , suggesting non-electrolyte complexes. The ligands and their complexes were characterized using spectroscopic techniques such as  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, FTIR, UV-Visible, CHN Elemental analysis, TGA/DSC Magnetic susceptibility and powdered x-ray diffraction. The data obtained from the elemental analysis (CHN) on the ligands and their complexes correlate well with stoichiometric composition of the compounds and are in good agreement with the theoretical values. The physio-chemical and analytical data of the ligands and complexes are presented in Table 1.



**Scheme 3:** Synthesis of the complex of HL2Cr, H2Co and HL2Fe where M stands for all the three metals



**Scheme 4:** Synthesis of the complexes of HL1Cr, HL1Co and HL1Fe where M stands for all the three metals

**Table 1: Physicochemical properties of Schiff Base Ligands and their Metal(III) Complexes**

Compound / Empirical Formula	Molecular mass (g/Mol.)	Colour	Melting point (°C)	Yield (%)	Elemental analysis Cal (Found)%				Molar conductivity (Scm <sup>2</sup> mol <sup>-1</sup> )	
					C	H	N	M		
HL1 (C <sub>17</sub> H <sub>13</sub> NO <sub>2</sub> )	(263)	Yellow	190-192	91 (0.240)	77.0 (77.01)	5.0 (5.03)	5.0 (5.06)	-	-	
HL2 (C <sub>17</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> )	(292)	Maroon red	100-101	93 (0.271)	69.0 (69.21)	4.01 (4.0)	10.11 (10.0)	-	-	
[CrL1] (CrC <sub>17</sub> H <sub>13</sub> NO <sub>2</sub> )	(314.99)	Yellow	240-241	79 (0.418)	52.0 (52.3)	3.12 (3.40)	3.44 (3.60)	13.50 (13.00)	15 x 10 <sup>-3</sup>	
[CrL2] (CrC <sub>17</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> )	(343.99)	Brown	250-251	81 (0.455)	49.30 (49.0)	3.50 (2.88)	7.14 (6.70)	13.00 (12.50)	12 x 10 <sup>-3</sup>	
[FeL1] (FeC <sub>17</sub> H <sub>13</sub> NO <sub>2</sub> )	(318.85)	Brown	233-235	73 (0.314)	52.9 (52.2)	3.04 (3.30)	4.00 (3.60)	14.00 (14.30)	17 x 10 <sup>-3</sup>	
[FeL2] (FeC <sub>17</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> )	(347.85)	Black	249-251	77 (0.353)	48.70 (48.60)	3.00 (2.90)	6.05 (6.70)	13.00 (13.30)	10 x 10 <sup>-3</sup>	
[CoL1] (CoC <sub>17</sub> H <sub>13</sub> NO <sub>2</sub> )	(321.93)	Red	200-203	90 (0.499)	51.40 (51.70)	3.04 (3.30)	3.40 (3.50)	13.50 (14.90)	6 x 10 <sup>-3</sup>	
[CoL2] (CoC <sub>17</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub> )	(350.93)	Green	237-238	79 (0.418)	48.10 (48.20)	3.00 (2.80)	7.00 (6.60)	13.00 (13.90)	12 x 10 <sup>-3</sup>	

M.p. = Melting point; Calc. = Calculated; g = Grams

### **Infrared spectroscopy**

plays a vital role in coordination chemistry, and it is one of characterization techniques that are used to confirm the formation of complex between ligands and metal ions. In order to verify the formation of complex, the infrared spectrum of ligand is compared with that of the complex. Herein, the infrared spectra of the ligands and their complexes were obtained in the region of 3500 – 500  $\text{cm}^{-1}$ . The data for some selected stretching bands are presented in Table 2. The spectra of the ligands showed a sharp and weak intensities bands at 1546.75 and 3119.15  $\text{cm}^{-1}$  for HL1 and sharp and medium bands at 1509.0-3473.0  $\text{cm}^{-1}$  for HL2, which are assignable to –NH and –OH characteristic bands presented in (Figure 7 and 8). The appearance of new band in all the complexes in region of 617  $\text{cm}^{-1}$  which are assignable to metal-oxygen band as reported in the literature of (Ashrafuzzaman, *et al.*, and Refat, *et al.*, 2021) further confirmed the formation of the complexes. A sharp stretching band at 1616 and 1620  $\text{cm}^{-1}$  are due to imine (C=N) band of the azomethine moieties within the ligands HL1 and HL2 shown in (Table 2). This band is the key indicator for the formation of Schiff bases (Savcı, *et al.*, 2021 and Suryawanshi, *et al.*, 2014). This band was observed to be weak and shifted to a frequency region of 3064, 3353  $\text{cm}^{-1}$  for the complexes of [CrL1] and [CrL2]. The shift in the band  $\nu(\text{O-H})$  may be due to phenolic coordination (Esther *et al.*, 2019). A sharp band was observed at the frequency of 1616 and 1628  $\text{cm}^{-1}$  as earlier mentioned, for the ligands synthesized, these bands shifted to a lower region at around 1592 and 1575,  $\text{cm}^{-1}$  for the complexes of [CrL1], and [CrL2]. This suggest imine  $\nu(\text{C=N})$  to metal (III) coordination (Ndahi and Nasiru 2012).

The strong sharp bands observed on the spectrum of the ligands at 1355, 1300, were assigned to  $\nu(\text{C-N})$ . A shift to higher region with some strong sharp intensities of 1381 and 1355  $\text{cm}^{-1}$  corresponding to [CrL1] and [CrL2].

A broad band appearing in the region 2331-2903  $\text{cm}^{-1}$  for both the Schiff base ligands and complexes is attributed to  $\nu(\text{C-H})$ , these could be due to the immense intermolecular hydrogen bonding within the aromatic chain (Suresh and Prakash 2010).

However, some new  $\nu(\text{M-N})$  bands with sharp intensities appeared in the FT-IR of the complexes, which happens to be absent in the spectrum of the synthesized Schiff base ligands. The  $\nu(\text{M-N})$  was observed at 466 - 483  $\text{cm}^{-1}$  for the complexes of chromium. This suggest coordination between metal ion and the lone pair of electrons on the nitrogen atom of the azomethine moiety (Fugu *et al.*, 2013). Iron(III) Complexes with the Schiff base Ligands (HL1, HL2). The weak bands, at the frequency of 3054 and 3476  $\text{cm}^{-1}$  in the IR spectra of the free ligands (HL1 and HL2) was assigned to hydroxyl  $\nu(\text{O-H})$  group as earlier indicated. In the spectra of the Fe(III) complexes, this band was shifted to higher frequency region in [FeL1] complex with a vibration band of 3282  $\text{cm}^{-1}$ , indicating coordination. In [FeL2], this band was observed to be broad and shifted to a lower frequency region of the with frequency of 3353  $\text{cm}^{-1}$ . The shift in frequency from ligand to the complexes in the iron complexes may be attributed to  $\nu(\text{O-H})$  coordination (Gabriel and Naomi, 2004).

As earlier pointed out, the  $\nu(\text{C=N})$  for the ligands (HL1 and HL2) appeared at 1616 and 1628  $\text{cm}^{-1}$  respectively. This band shifted to a lower region at around 1522 and 1610  $\text{cm}^{-1}$ . This suggest coordination of the azomethine nitrogen to the metal ions (Ndahi and Nasiru, 2012). The  $\nu(\text{C-N})$  bands assigned to the Schiff base ligands shifted to a higher region with some strong sharp intensities of 1372 and 1355  $\text{cm}^{-1}$  corresponding to [FeL1] and [FeL2]. However, this assignment is similar to those observed by (Fugu *et al.*, 2012).

A weak band was observed at  $\nu(\text{C-N})$  for the Schiff base ligands and their iron (III) complexes ranging from  $2331\text{-}2675\text{cm}^{-1}$ , which was assigned to the aromatic bands. The coordination through azomethine  $\nu(\text{C=N})$  and carbonyl oxygen  $\nu(\text{C-O})$  of ligands are further evidenced by the appearance of non-ligand bands in the complexes around  $589\text{-}492$  and  $600\text{-}500\text{ cm}^{-1}$  assigned to  $\nu(\text{M-N})$  and  $\nu(\text{M-O})$  for the Iron (III) complexes of [FeL1 and FeL2], respectively (Suresh and Prakash, 2010; Ali *et al.*, 2017).

Some sharp bands were also observed at  $747$ ,  $738$ ,  $747$ , and  $747\text{cm}^{-1}$  for the complexes of [FeL1] and [FeL2], whereas these bands were not observed in the spectra of the ligands. This indicate that the metal ions are coordinated through the phenolic oxygen atom  $\nu(\text{M-O})$  of the Schiff base ligands (Esther *et al.*, 2019). In the Cobalt Complexes with the Schiff base Ligands HL1 and HL2, the  $\nu(\text{O-H})$  bands observed was broad which show a broad intensity band at a wavelength of  $3362\text{ cm}^{-1}$  and shifted to lower frequency compared to the frequency of the ligand in the infrared spectrum. Compound [CoL2] shows a sharp intensity band, and shifted to lower frequency with a vibration band of  $3353\text{cm}^{-1}$ . In the spectrum of [CoL1] the bands were observed to be sharp and shifted to a higher frequency region of the infrared spectroscopy with wavelength of  $3353$  and  $\text{cm}^{-1}$ .

In the FT-IR spectrum of the free ligands, HL1 and HL2, a strong and sharp band at around  $1616$  and  $1628\text{ cm}^{-1}$  region which corresponds to, the imine, azomethine  $\nu(\text{C=N})$  stretching vibrations which shifted to a lower region at around  $1610\text{cm}^{-1}$  for all the two cobalt complexes (Ndahi and Nasiru 2012).

The synthesized Schiff base ligands shows a strong sharp band at  $1355$  and  $1366\text{ cm}^{-1}$  for HL1 and HL2. The spectra of the cobalt(III) complexes shifted to higher region with some strong sharp intensities of  $1381$  corresponding to [CoL2]. Compound [CoL1] shifted to lower frequency of  $1346\text{cm}^{-1}$  with a sharp band compared to the band intensity of the ligand, which were attributed to  $\nu(\text{C-N})$  (Fugu *et al.*, 2013).

A weak band was observed at the vibrational band of  $\nu(\text{C-H})$  aromatic, of the Schiff base ligands and their cobalt(III) complexes ranging from  $2331\text{ - }2675\text{ cm}^{-1}$  in the spectral data of all the Schiff base ligands and their metal (III) complexes (Suresh and Prakash 2010).

New  $\nu(\text{M-N})$  bands with sharp band intensities appeared in the complexes, which happens to be absent in the spectrum of the synthesized Schiff base ligands. The  $\nu(\text{M-N})$  was observed at  $642$  and  $474\text{ cm}^{-1}$  for the complexes of cobalt, [CoL1] and [CoL2]. This is due to metal to nitrogen bonds, suggesting coordination between metal ion and the lone pair of electrons on the nitrogen atom of the azomethine moiety (Gabriel and Naomi, 2004, Ali *et al.*, 2017).

Strong sharp bands were also observed at  $718$  and  $738\text{ cm}^{-1}$  for the complexes of [CoL1] and [CoL2], whereas these bands were not observed in the spectra of the ligands. This indicate that the metal ions are coordinated through the phenolic oxygen atom  $\nu(\text{M-O})$  of the Schiff base ligands (Esther *et al.*, 2019).

Table 2: Infrared spectral data of the ligands and their complexes

Compounds	$\nu(\text{O-H})$	$\nu(\text{C=N})$	$\nu(\text{C-N})$	$\nu(\text{C-H})$ Aromatic	$\nu(\text{M-O})$	$\nu(\text{M-N})$
HL1	3054w	1616s	1355s	2649w	-	-
HL2	3476w	1628s	1300w	2366w	-	-
HL3	3062w	1610s	1311s	2340w	-	-
HL4	3440b	1619s	1328s	2331b	-	-
[CrL1]	3054w	1592s	1381s	2323w	747s	466s
[CrL2]	3353s	1575s	1355s	2331b	738s	466s
[FeL1]	3282w	1522s	1372s	2331w	747s	589s
[FeL2]	3353b	1610s	1355s	2349w	738s	492s
[CoL1]	3353s	1610s	1346s	2331w	718w	642w
[CoL2]	3353s	1610s	1381s	2340w	738s	474s

### Electronic spectral study

To establish the formation of the complexes, electronic spectral study was carried out on the free ligands and their complexes. The spectra of the ligands displayed absorption bands at 314–361 nm for HL1 and 316–361 nm for HL2 respectively presented in Table 3. These peaks can be attributed to  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  within the aromatic moiety and azomethine group respectively (Abbas, 2016). The UV-Visible electronic spectra of the free ligands and their metal complexes were recorded in ethanol at room temperature in the wavelength range of 800 – 200 nm. The peaks due to aromatic are observed in the region of 200- 290 nm, which can be ascribed to the  $\pi \rightarrow \pi^*$  intra ligand charge transfer transitions and is related to transition of ethereal oxygen of the ligands, due to the conjugation in the ligand molecules. The  $n \rightarrow \pi^*$  transitions, are assigned to molecules transiting at 300, 370, and 390 nm. This transition is due to azomethine moiety in the ligands which may shift in the wavelength of the complexes indicating metal to nitrogen imine group (M-N) coordination. The peaks in the complexes at 300 to 390 nm could be due to LMCT or MLCT transitions depending upon the nature of the ligands coordination to form the complexes. This is ascribed to (M-N) indicating metal to nitrogen bond (Buyukusulu *et al.*, 2010). The absorption band of the complexes have bathochromic or hypsochromic shift compared to those of the ligands (Manonmani *et al.*, 2001). Electronic Spectral data of Chromium(III) Complexes with the Schiff base Ligands, the electronic spectra of the free ligands (HL1 and HL2) showed a band at around 315 – 485nm presented in Table 3. The electronic spectrum of the chromium complex [CrL1], showed the appearance of a band at 360 nm and absent in the spectrum of the free ligand which is attributed to  ${}^4A_{2g} \rightarrow {}^4T_{1g}(P)$  transition which was ascribed to M-N bond, indicating coordination of the metal ion with nitrogen atom of the imine group (Nath and Chaundhary, 1999).

Similarly, the appearance of a strong band at 511 nm in the spectrum of the complex [CrL1], which was not found in the spectrum of the free ligand, was assigned  ${}^4A_{2g} \rightarrow {}^4T_{2g}(F)$  transition, ascribed to (M-O) bond (Natarajan, 1977; Sonmez and Sekerci, 2002). For complex [CrL2], a well-defined band appeared at 367 nm ascribed to  ${}^4A_{2g} \rightarrow 3T_{2g}$  transition this showed a shift toward lower wavelength compared to the wave length of the ligand which was 464 nm, this indicates a bond at the azomethine nitrogen atom (M-N). The (M-O) bond in the complex [CrL2] was observed, by the appearance of a sharp band shifted toward a longer wavelength at 515 nm due to  ${}^4A_{2g} \rightarrow {}^4T_{2g}(F)$  transition (Pedro *et al.*, 2006). This suggest an octahedral



geometry for the chromium compounds, and agrees with their magnetic moments values which ranges from 3.20 – 3.82 B.M

Electronic Spectral data of the Iron(III) Complexes with Schiff base Ligands (HL1 and HL2), in this class of compounds, the band appearing in the range of 314 – 315 is attributed to  $\pi-\pi^*$  of the ligands. In the spectra of the complexes, these bands are slightly shifted to a lower wavelength (314-316 nm). The bands in the range 351-371 nm in the ligands are assigned to  $n-\pi^*$  transitions of the azomethine group. In the complexes, these bands shifted to 363-367 (blue shift), suggesting that the nitrogen atom of the azomethine group is coordinated to the metal ion. Absorption bands at 452 and nm in the complexes [FeL1 and FeL2] respectively are attributed to MLCT and  ${}^5T_{2g}(F) \rightarrow {}^5T_g$  transitions which is compatible to high-spin octahedral geometry for Iron (III) complexes (Canpolar,2005). Their magnetic moment values observed in the range of 5.0 – 5.98 B.M confirms this assignment. Electronic Spectral data of Cobalt(III) Complexes with the Schiff base Ligands with bands appearing in the range of 314 – 315 is attributed to  $\pi-\pi^*$  and from 315-385 nm are attributed to  $n-\pi^*$  transitions. There was a band shift at 367 and 490 nm showing a bathochromic shift of the cobalt(III) complex of [CoL1], compared to the wavelength of the ligands which was due to  ${}^4T_{1g} \rightarrow {}^4A_{2g} V_2$  and  ${}^4T_{1g} \rightarrow {}^4T_{1g} V_3$  transitions indicating a bond at nitrogen and oxygen atoms of the ligand to form the complex. The complex compound of [CoL2], showed a sharp band shifted toward lower wavelength at 364 nm indicating the azomethine bond while the formation of phenolic oxygen bond was observing by the sharp band appearing at 468 nm which moves toward higher wavelength, attributed to  ${}^4T_{1g} \rightarrow {}^4A_{2g} V_2$  and  ${}^4T_{1g} \rightarrow {}^4T_{1g} V_3$  transitions respectively. This is due to less excitation of the d-electrons, (Nath and Chaundhary,1999). A shift toward a lower wavelength at the 463 nm assigned to  ${}^4T_{1g} \rightarrow {}^4T_{1g} V_3$  transition, indicates the bond at the oxygen atoms of the ligands to the central cobalt ion, all complexes are suggested to have octahedral geometry (Naomi and Gabriel, 2005. Their magnetic moment values were observed in the range of 4.0 – 3.9 B.M which agrees with high spin Cobalt (III) complexes.

**Table 3: Electronic spectral data of the ligands and their complexes**

Compounds	Wavelength(nm)	Wavenumber( $cm^{-1}$ )	Band assignment
HL1	315	31746	$\pi - \pi^*$
	351	28490	$n - \pi^*$
	371	26954	"
HL2	314	31847	$\pi - \pi^*$
	370	27027	$n - \pi^*$
	464	21551	"
[CrL1]	316	31645	${}^4A_{2g} \rightarrow {}^4T_{1g}(P)$
	360	27777	"
	511	19569	${}^4A_{2g} \rightarrow {}^4T_{2g}(F)$
[CrL2]	315	31746	${}^4A_{2g} \rightarrow {}^4T_{1g}(P)$
	367	27247	${}^4A_{2g} \rightarrow {}^3T_{2g}$
	515	19417	${}^4A_{2g} \rightarrow {}^4T_{2g}(F)$
[FeL1]	316	31645	MLCT
	367	27247	MLCT
	452	22123	${}^5T_{2g}(F) \rightarrow {}^5F_g$
[FeL2]	315	31746	${}^6A_{2g} \rightarrow {}^4T_{2g}$
	363	27548	MLCT
	444	22522	${}^5T_{2g}(F) \rightarrow {}^5F_g$
	490	20408	${}^4T_{1g} \rightarrow {}^4T_{1g} V_3$
[CoL1]	314	31847	${}^4T_{2g} \rightarrow {}^4T_{2g} V_1$
	367	27247	${}^4T_{1g} \rightarrow {}^4A_{2g} V_2$
	490	20408	${}^4T_{1g} \rightarrow {}^4T_{1g} V_3$
[CoL2]	315	31746	${}^4T_{2g} \rightarrow {}^4T_{2g} V_1$



364	27472	${}^4T_{1g} \rightarrow {}^4A_{2g} V_2$
468	21367	${}^4T_{1g} \rightarrow {}^4T_{1g} V_3$

### Thermo-gravimetric analysis for the Chromium, Iron and Cobalt (III) Complexes

The thermo-gravimetric analysis of the compounds gives an information on the water of hydration in the coordination sphere of the central metal ion, and the scheme of thermal decomposition of the complexes. The two ligands showed decomposition at temperature ranging from 102 - 574°C, with a weight loss ranging from 5.19 – 19.07 % (calculated at 5.44 – 18.0%), indicating some phenyl groups have decomposed, it was considered that some molecules of water, hydrogen, chloride and molecules of phenyl groups have decomposed in all the complexes. The thermal stability of the Cr(III), Fe(III) and Co(III) complexes synthesized was carried out under nitrogen atmosphere at 25 -800°C using heating range of 30 °C/min, all the ligands showed decomposition at temperature ranging from 102 - 574°C, with a weight loss ranging from 5.19 – 19.07 % (calculated at 5.44 – 18.0%), indicating some phenyl groups have decomposed. The complexes also showed decompositions with a weight loss. The results obtained from thermal analysis are consistent with the proposed theoretical formula of the elemental analysis (Ali *et al.*, 2018). Thermo-gravimetric analysis for the Chromium (III) Complexes of CrL1 and CrL2 showed decomposition at temperatures ranging from 48.22 – 298.65 °C with a weight loss ranging from 13.02 – 33.56 % (calculated as 11.22- 33.55%). These weight losses at this temperature corresponds to the loss of molecules of water. The second decomposition stage were observed at the range of 100.55 - 608.71°C on the thermogram of the complexes, with a weight loss of 4.21 – 42.77% (calculated as 4.19 – 42.78%). The decomposition is assigned to the loss of organic (Ligand) and chlorine molecules within the complexes. The third decomposition stage were also observed at temperature ranging from 189.03 – 628.83 °C for all the chromium complexes representing decomposition of the chromium metal ions (Samar,2018). Thermo-gravimetric analysis for the Iron (III) Complexes of FeL1 and FeL2 showed an endothermic peak at temperature ranging from 47.63- 366.89 °C at the stage one decomposition temperature which were assigned to loss of water molecules, with sample weight loss ranging from 3.01 – 26.25%(calculated 1.67 -26.20 %). The second stage of decomposition of the iron complexes showed an endothermic peak also at temperature ranging from 125.72 -521.13°C which indicates that the compounds have less thermal stability, with weight loss ranging from 11.10-27.82 % (calculated 11.33- 27.20%). These indicates the loss of some organic and halogen molecules. The decomposition of the iron metals was observed at the range of 363.14 – 765.72°C with weight loss range at 39.78- 55.34% (calculated 41.58-55.42%) (Samar,2018). Thermo-gravimetric analysis for the Cobalt (III) Complexes showed three stages of melting and decomposition processes at 49.55- 260.93°C temperature range for the first stage with weight loss range at 2.15 - 25.71 % (calculated 2.05 - 25.68%), these may be due to loss of water molecule, the second stage showed a decomposition temperature at 110.10 – 420.26°C temperature range with weight

loss of 3.01 - 16.30 % (calculated 2.99 - 16.20%), these were also due to the loss of organic molecules as well, the third decomposition stage was observed at the range of 179.04 -806°C with weight loss at the range of 34.54 – 52.69% (calculated 21.99 – 52.68%), Cobalt ions were expected to decompose at these temperature range (Alireza *et al.*, 2016).

**Table 4: Thermo-gravimetric data of the ligands and their complexes**

No	Compound	Stage	TG/°C	Mass lost % Found	Mass lost % Cal	leaving Species
[HL1]	I	189- 412		8.63	8.53	C <sub>6</sub> H <sub>5</sub> NH
[HL2]	I	102-574		19.07	18.0	C <sub>6</sub> H <sub>5</sub> NH
[CrL1]	I	54.38-250.18		-17.66	-17.63	-H <sub>2</sub> O
	II	250.69-393.67		14.54	14.56	Cl
	III	394.16-628.83		49.79	49.78	
[CrL2]	I	48.91-100.55		13.02	11.22	-H <sub>2</sub> O
	II	100.55-188.53		17.20	17.19	
	III	189.03-628.92		49.83	49.79	
[FeL1]	I	56.65-366.89		3.01	1.67	-H <sub>2</sub> O
[FeL2]	I	144.21-267.41		9.65	9.67	-H <sub>2</sub> O
	II	267.41-488.37		11.10	11.33	Cl
	III	491.87-736.36		46.07	46.11	
[CoL1]	I	56.29-166.78		4.70	4.72	-H <sub>2</sub> O
	II	166.78-402.29		14.59	14.59	Cl
	III	403.26-771.20		52.69	52.68	
[CoL2]	I	97.15-260.43		15.04	15.10	-H <sub>2</sub> O
	II	260.93-420.26		15.08	15.10	
	III	241.25-806.17		34.54	21.99	Cl

### Magnetic susceptibility

The room temperature magnetic moment of the chromium (III) complexes are presented in Table 5 where the values obtained ranges between 3.20 – 3.82 B.M. The outer electronic configuration of chromium is 3d<sup>3</sup> in the high spin complexes, where the number of unpaired electrons in t<sub>2g</sub> orbitals is 3, The calculated and experimental magnetic moment values of the complexes were observed to be specific for octahedral geometry complexes (Anastasiadis *et al.*, 2013).

Iron complexes have the magnetic susceptibility values ranging from 5.0 -5.98 B.M, and are high-spin octahedral complexes. The calculated and experimental magnetic moment values of the complexes were observed to agree with high spin octahedral geometry as reported by Pramanik and Modal, (2014).

The cobalt complexes show a magnetic susceptibility values ranging from 3.74 – 4.02 B.M. This indicates that the complexes are high spin octahedral complexes(<sup>5</sup>T<sub>2g</sub>) (Figgis and Lewis,1964). The calculated and experimental magnetic moment values of the complexes

were observed to be in agreement for octahedral geometry complexes according to (Pramanik and Modal, 2014).

### **Nuclear Magnetic Resonance (NMR)**

Nuclear magnetic resonance(NMR) is an analytical technique that elucidate or provide detailed information about molecular structure and also a primary quantitative method allowing the determination of concentration of molecules even in complex mixture in addition to the well- known observation of hydrogen, carbon, fluorine and phosphorus and a number of other elements (Kemp, 1981).

### **Proton Nuclear Magnetic Resonance (<sup>1</sup>H NMR)**

The <sup>1</sup>H NMR is a probe used to examine the structure of molecules in the application of nuclear substance (Adem *et al.*, 2011). The <sup>1</sup>H NMR of the synthesized free ligands and the metal (III) complexes were recorded in deuterated dimethylsulfoxide (DMSO), the chemical shift were recorded in ppm and presented in Table5. The <sup>1</sup>H NMR spectrum of the free Schiff base ligands (HL1 and HL2). The spectra showed a sharp singlet peaks at  $\delta$  :15.59 ppm for HL1, while HL2 show a sharp single peak at  $\delta$  :11.92 ppm representing the enolic (C=C-OH) group proton, these protons appeared in the downfield region due to the electronegative effect of the oxygen atom which causes the proton to be de-shielded and subsequently occur in the down field region (Waziri *et al.*, 2022). The aromatic proton (C-H) appeared at  $\delta$  : 6.65 and 8.26 ppm as a sharp singlet and doublets peaks for the ligands (HL1 and HL2) respectively, and the azomethine proton (HC=N) appeared as a singlet peak at around  $\delta$  :10.30 and 10.78 ppm in the spectrum for the Schiff base ligands (HL and HL2) respectively as well. These values are in agreement with literature (Ali *et al.*, 2017; Bushra *et al.*, 2018; Duke-eze *et al.*, 2011). There is also appearance of a single sharp peak at  $\delta$  3.0 -3.68 ppm in all the spectra, which is due to the the DMSO solvent that was used for the NMR analysis.<sup>13</sup>C NMR of the Schiff Base Ligands (HL1 and HL2)

Carbon NMR is analogous to proton NMR and is used for the identification of carbon atoms in a molecule just as proton NMR identifies atoms. It also ascertains how atoms within a particular molecule are related. This is achieved by analyzing chemical domain of the selected nucleus (Waziri *et al* 2022). The carbon <sup>13</sup>C NMR spectra of the Schiff base ligands (HL1 and HL2) were determined in deuterated dimethylsulfoxide (DMSO) and reported in ppm, these are presented in Table 5. In the spectra of the synthesized Schiff base ligands HL1 and HL2, the enolic oxygen (C=C-OH) were observed in the downfield region at  $\delta$  163.65 and  $\delta$  169.97 ppm, for HL1. In the same manner, the azomethine (HC=N) carbon was observed at around  $\delta$  149.89 and 146.46 ppm for the Schiff base ligands (HL1 and HL2) respectively (Gichumbi *et al.*, 2016). Aromatic carbon shows a peak at around  $\delta$  108-138 and  $\delta$  113-137 ppm at the down field region for all the two respective ligands. In all the spectra of the ligands, the appearance of an intense peak in the region 39.08-39.72 is assigned to the DMSO peak.

<sup>1</sup>H NMR of the Chromium(III) Complexes with the Schiff base Ligands presented in Table 5, the enolic (C=C-OH) and the azomethine (HC=N) proton that appeared downfield in the spectrum of the free ligands did not appear on the spectra of the complexes of chromium. The disappearance of these protons in the complexes confirmed the deprotonation of the protons and coordination of the Cr(III) ion to the ligand through the oxygen and the nitrogen atom of the hydroxyl and imine azomethine groups, and the aromatic proton were significantly shifted

in the spectrum of the complexes (Waziri *et al.*, 2022). Solvent peaks were observed in the range of  $\delta$  3.33 – 3.38 ppm.

The  $^1\text{H}$  NMR spectra of the iron(III) complexes shows the enolic (C=C-OH) proton, which appeared downfield in the spectrum of the free ligands and did not appear on the spectra of the complexes of the iron complex. The disappearance of these protons in the complexes confirmed the deprotonation of the protons and coordination of the Fe(III) ion to the ligand through the oxygen atom of the hydroxyl group. In addition, the azomethine and the aromatic protons show a weak peak which significantly shifted in the spectrum of the complexes to  $\delta$  10.77 and 10.66, ppm for [FeL1 and FeL2] respectively for the azomethine protons. This shift in the chemical environment of the azomethine proton is due to the involvement of the nitrogen atom in the coordination (Waziri *et al.*, 2022). Peaks of solvent (DMSO) were observed in the range of  $\delta$  3.29 – 3.36 ppm. The  $^1\text{H}$  NMR spectra of the Co(III) complexes shows that the enolic (C=C-OH) and the azomethine (HC=N) proton appeared downfield in the spectrum of the free ligands did not appear on the spectra of the complexes of cobalt as well. The disappearance of these protons in the complexes confirmed the deprotonation of the protons and coordination of the Co(III) ion to the ligand through the oxygen and the nitrogen atom of the hydroxyl and imine azomethine groups.

## PXRD

### Powdered X-ray diffraction analysis for the Chromium, Cobalt and Iron (III) Complexes

Several attempts were made toward obtaining a single crystal for SCXD analysis, which was unsuccessful. Hence, powder x-ray diffraction analysis (PXRD) was carried out on the compounds. This is an important tool for identifying and characterizing crystalline or amorphous materials/compounds. Crystalline materials show sharp peaks under powder x-ray diffraction, and amorphous materials or compounds show broad background signals (Gonon, *et al.*, 2020).

From the diffraction patterns obtained, it can be seen that some of the complexes exhibit sharp peaks, and this suggests that they are crystalline. The  $[\text{Cr}^{3+} \text{ L1 and L2}]$  complexes exhibited a broad signal, which indicates their its amorphous nature.

Powdered X-ray diffraction analysis for the Iron (III) Complexes shows the appearance of (XRD) spectra of four intense peaks from compound FeL1 and FeL2 at peak locations of ( $2\theta = 31.8$ ) and ( $2\theta = 25.6$ ), with the narrowed inter-planer d-spacing of 2.81 and 3.47 (found) and 2.82 and 3.50 (calculated) respectively (Table 5). All the complexes of iron gave a homogeneous large crystalline structure, of 59.4 and 37.7 nanocrystal

All the two cobalt complexes are crystalline with a large crystal size of 27.1 and 34.6 nm corresponding to CoL1 and CoL2. The intense peaks observed at the spectrum of the complexes were positioned at angle ( $2\theta = 25.6$  and  $5.18$ ) for the complexes FeL1 and FeL2 respectively. The grain within the complexes were situated at a narrowed inter-planer spacing of 3.47 and 17.0 (Found) which corresponds to the calculated values of 3.53 and 17.1.

**Table 5: Powdered X-ray diffraction data for the Ruthenium (III) Complexes**

cpds	K	$\lambda(\text{\AA})$	$2\theta$ ( $^\circ$ )	FWHM( $\beta$ )	d( $\text{\AA}$ )		D(nm)
					Found	Calc	
[CrL1]	0.94	1.5406	-	-	-	-	-
[CrL2]	"	"	-	-	-	-	-
[FeL1]	"	"	31.80	0.14	2.81	2.82	59.4

[FeL2]	“	“	26.5	0.22	3.47	3.50	37.7
[CoL1]	“	“	25.6	0.30	3.47	3.53	27.6
[CoL2]	“	“	5.18	0.24	17.0	17.1	34.6

Key: FWHM =full width at half maximum, d =inter-planer spacing between the grains, D = crystallite size,  $\theta$  = angle of diffraction, k = Sherrer constant,  $\lambda$  = wavelength of diffraction.

**Virtual screening and molecular docking analysis for the Schiff base ligands HL1 and HL2 and their Chromium, Cobalt and Iron complexes with GS *Mycobacterium Tuberculosis* protein**

Structural analysis of GS from *mycobacterium tuberculosis* (MTB) revealed that it has three domains. Domain I or N-terminal domain, Domain II or Central domain and Domain III or C-terminal domain. These domains belong to alpha and beta ( $\alpha/\beta$ ) class (White *et al.*, 2004; Kotnik *et al.*, 2007). The enzyme has three binding sites, namely; substrate binding site, ATP binding site and glutamic acid binding site. Inhibition of any of these residues involved in the above-mentioned binding sites would hinder the activity of the enzyme. Virtual screening of small compound libraries may provide novel inhibitors that have the potential to be used as drugs in future. Despite the availability of several methods, virtual screening remains the best method that efficiently provides suitable ligands from large compound libraries for a biological assay (Wu *et al.*, 2012). The result of molecular docking studies of the ligands against GS revealed that the ligands underwent various non-covalent interactions such as hydrophobic interaction, electrostatic interaction where the residues are, Phe 268, leu 267, Leu 369, Val 363, Val331, Gly 143, Try 210, Try 219, Pro266, Lys 249, Lys 294, Glu 145, His 324 and Try142 and hydrogen bonds interactions as presented in figure1- 16 below. Therefore, all the ligands had essential activity against the normal function of GS protein, the ligand CoL1, have higher activity on the enzyme, with minimum inhibition concentration constant of 4.44  $\mu\text{m}$  based on the *in-silico* molecular docking studies. Results presented in Table 6.

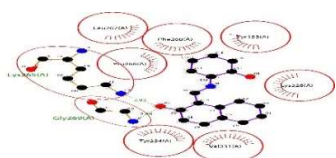


Figure 1: HL1 hydrophobic interaction with GS

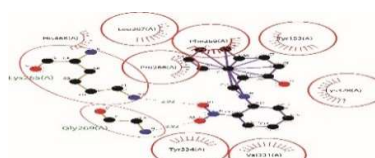


Figure 2: HL2 hydrophobic interaction with GS

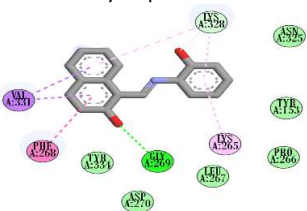


Figure 3: HL1 hydrogen bond interactions with GS

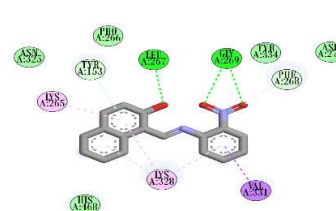


Figure 4: HL2 hydrogen bond interactions with GS

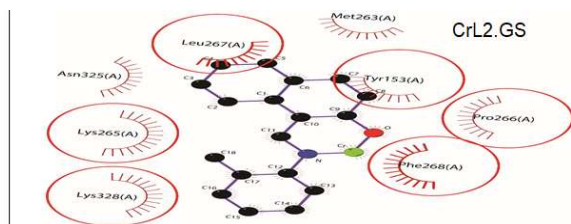
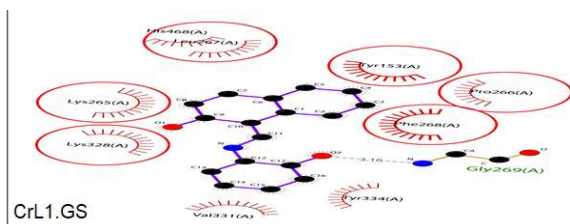




Figure 5: CrL1 hydrophobic interactions with GS

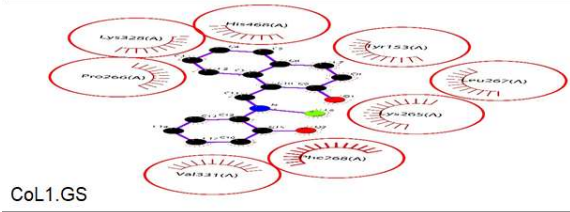


Figure 6: CrL2 hydrophobic interactions with GS

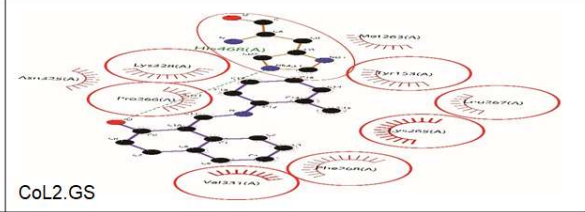


Figure 7: CoL1 hydrophobic interactions with GS

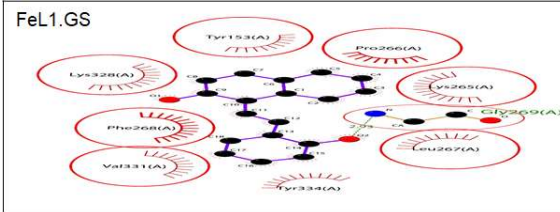


Figure 8: CoL2 hydrophobic interactions with GS

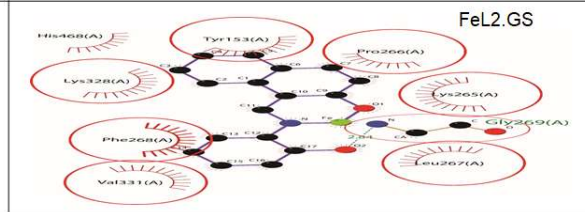


Figure 9: FeL1 hydrophobic interactions with GS

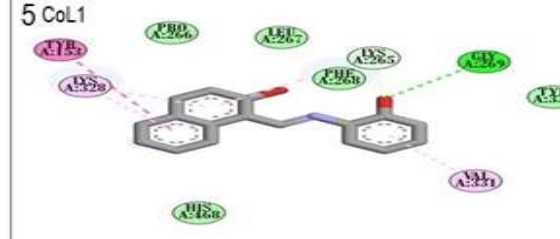


Figure 10: FeL2 hydrophobic interactions with GS

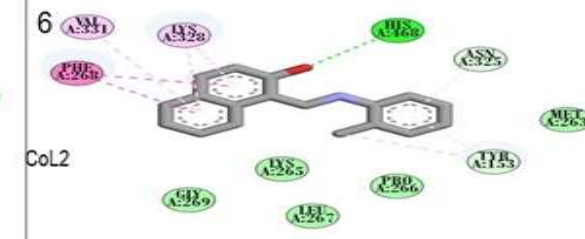


Figure 11: CoL1 hydrogen bond interactions with GS

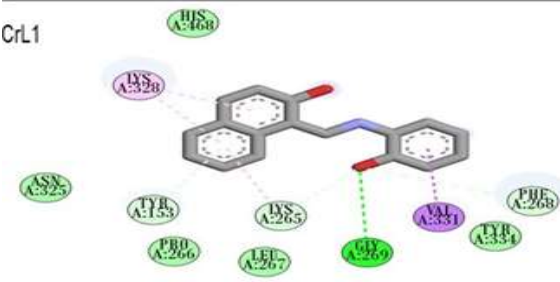


Figure 12: CoL2 hydrogen bond interactions with GS

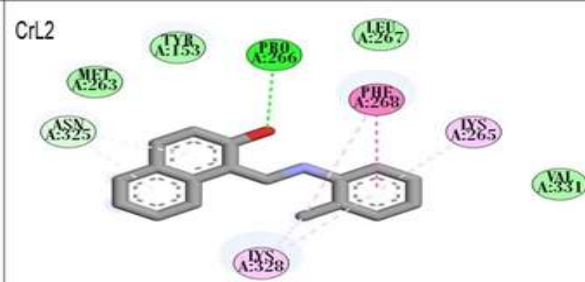


Figure 13: CrL1 hydrogen bond interactions with GS

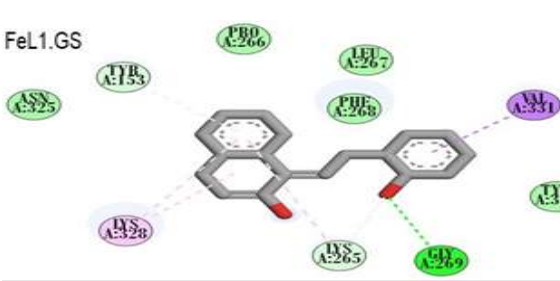


Figure 14: CrL2 hydrogen bond interactions with GS

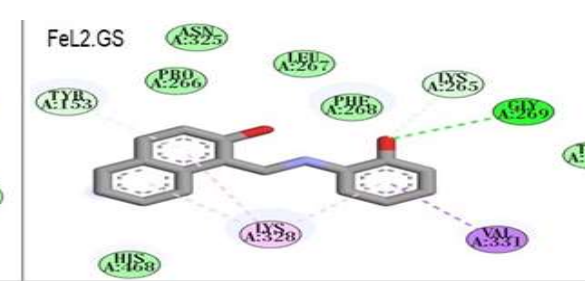


Figure 15: CoL1 hydrogen bond interactions with GS

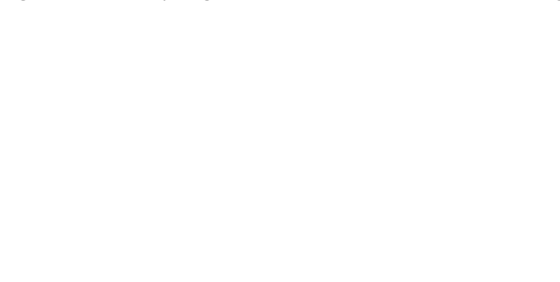
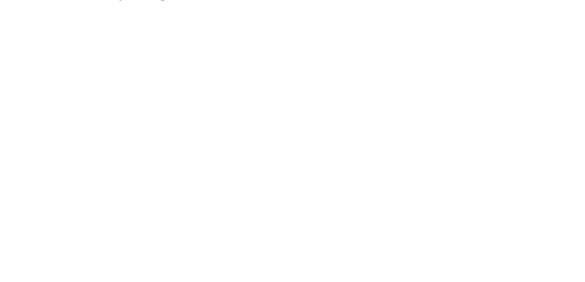


Figure 16: CoL2 hydrogen bond interactions with GS



**Table 6: Molecular docking data for the Schiff base ligands and their Chromium, Cobalt and Iron(III) Complexes**

Cpds	FreeBinding Energy/Docking Scores	Hydrogen bond	Bond Distance (Å)	Hydrophobic interaction	Vander Waals Interaction	Inhibition concentration Constant(µM)
[HL1]	-7.12	Lys 265 Gly269	2.93 2.69	Leu267 Phe268,Phe268	Tyr334,Gly269,Lys 265,Leu267,Pro266 Phe268,Tyr153,Lys326 Val331.	6.07
[HL2]	-7.59	Lys 265 Gly269	2.92 2.82	Leu267 Phe266	Gly269,Lys265,His468 Leu267,Pro266,Phe268 Tyr153,Lys328,Val331 Tyr334.	2.72
[CrL1]	-6.92	Lys 265 Gly328	2.61 2.56	Leu267, Phe268,	Lys328,Lys268His468, Lys167,Tyr153,pro266 Phe268,Gly269,Tyr334 Val331	8.48
[CrL2]	-6.92	Lys328	3.01	Leu267, Phe268,	Lys328,Lys265,Asn325,Le u267Met263,Tyr153,Pro2 66,Phe268	28.89
[FeL1]	-6.51	Gly269	3.16	Phe268,	Val331,Phe268,Lys328,Ty r153,Pro266Lys265Gly26 9,Leu267,Tyr334	16.82
[FeL2]	-6.83	Gly 269	2.16	Phe268,	Val331,Phe268,Lys328,Hi s468,Tyr153,Pro266,Lys2 65Gly269,Leu267	9.78
[CoL1]	-7.30	Gly269	2.93	Phe268,	Pro266,Lys325,His468,Tyr 153Leu267,Tyr265Lys265 ,Pro266 Val331	4.44
[CoL2]	-6.74	Gly328	2.84	Phe268,	Pro266,Asn328,Lys224,Hi s468,Met263,Tyr158Leu2 67,Tyr268His268,Val381	11.56

**Physicochemical properties of the Schiff base Ligands and their Chromium, Cobalt and Iron (III) Complexes**

The physicochemical properties were assessed for Schiff base ligands and their metal(III) complexes, and it was found to have good oral bioavailability and shows desirable drug-likeness as presented in (Table7). The results are consistent with Lipinski's rule of five which shows that the molecular weight of all the compounds is compatible with the upper limits 500 g/mol. as outlined by (Lipinski, *et al.*, 2001). The solubility of all the compounds (WLogP) are also within the recommended value ranging between 3.26- 4.30, which is less than 5, according to Muegge rule. The hydrogen acceptors are also in consistent with the Muegge rule, which accept less or equal to 10 number of hydrogen atom for a compound that has good drug likeness. Where the hydrogen donor atoms found in the compound are also in good agreement with the number of atoms design by Muegge rule (Muegge *et al.* ,2001) which is less or equal to 5 hydrogen donor atoms, found in the compound are all less than 5. Pan assay interference structure of all the compound gave a zero alert which is in accordance with Baell rule (Baell, 2010 ; Mustafa, 2020)that means it maintained zero (0) alert to (PAINS) and did not receive an alert as a potential inhibitors. Number of rotational bonds of all the compounds are less than 10 which obeys the Veber rule (Veber, *et al.*, 2002). The topological surface area of the compound obeys the Veber rule, which is well within the suggested general upper limit



of 140 Å<sup>2</sup>, and values ranges between 21.70 -78.41. All the compounds show a good absorption values ranging from 80.09 – 96.68 for the molar refractivity.

**Table 7: Physicochemical properties of the Schiff base Ligands and their Metal (III) Complexes**

S/No.	Compounds	Molecular Weight (≤500)	WLog P (≤ 5)	H-Bond Acceptor (≤ 10)	H-Bond Donor (≤ 5)	PAINS	Molar Refractivity (≤130)	Num. rotatable bonds(≤10)	TPSA (≤140)
1	[HL1]	263	3.96	3	1	0	96.68	3	42.85
2	[HL2]	292	4.20	4	1	0	88.49	3	78.41
3	[CrL1]	314.28	3.46	2	0	0	80.97	0	21.70
4.	[CrL2]	343.28	3.44	3	0	0	90.42	2	58.06
5	[FeL1]	318.13	3.46	2	0	0	80.97	0	21.70
6	[FeL2]	347.13	3.44	3	0	0	90.48	2	58.06
7	[CoL1]	321.22	3.46	2	0	0	80,97	0	21.70
8	[CoL2]	350.21	3.44	3	0	0	90.42	2	58.06

Key: WLog p = Water solubility, PAINS = Pan assay interferences, TPSA =Topological Polar Surface Area

**Pharmacokinetics properties of the Schiff base Ligands and their Metal (III) Complexes**

The pharmacokinetics properties were evaluated for Schiff base ligands and their metal (III) complexes, which confirms that all the compounds have good oral and desirable drug-likeness properties, results are presented in (Table 8). The findings align with Lipinski's rule of five, were expected good intestinal absorption was accompanied by the molecules with a topological polar surface area value below 140. The result indicates that the compounds have the ability to cross blood–brain-barrier, (BBB), This indicates a good potential permeability through cellular plasma membranes. Also, according to Lipinski, the probability of being absorbed depends upon the molecular hydrophilic (WLogp ) value. On the basis of this, the compound was found to be within the acceptable range presented in (Table 8). The results suggest that the compound has high potential to be absorbed in the intestine (HIA+). The compounds have not received an alert as a potential inhibitor of CYP2D6 by the human liver presented in (Table 8). On the other hand, toxicity, Mutagenicity, Tumorigenicity, Irritability, Reproducibility, and Carcinogens analysis were carried out for all the selected ligands. Based on the toxicity studies all the four (4) compounds were non-toxic. Thus, the compound possesses desirable pharmacokinetics properties and can be considered as a drug-like compounds.

**Table 8: Pharmacokinetics properties of the Schiff base Ligands and their Metal (III) Complexes**

S/No.	Compounds	Blood-Brain Barrier	Human Intestinal Absorption	CYP450 2D6 Inhibitor	Carcinogens	Mutagenic	Tumorigenic	Reproductive Effect	Irritant
1.	[HL1]	BBB+	HIA+	Non-inhibitor	Non-carcinogens	None	None	None	None
2.	[HL2]	+	+	“	“	None	None	None	None
3	[CrL1]	+	+	“	“	None	None	None	None
4	[CrL2]	+	+	“	“	None	None	None	None
5	[FeL1]	+	+	“	“	None	None	None	None
6	[FeL2]	+	+	“	“	None	None	None	None
7	[CoL1]	+	+	“	“	None	None	None	None
8	[CoL2]	+	+	“	“	None	None	None	None

Key: CYP4502D6 = Liver absorptivity

## CONCLUSION

In this research work, two different bidentate Schiff base ligands and their chromium, Cobalt and iron (III) metal complexes were synthesized, characterized and designed as antitubercular drugs. Complexes were afforded by the condensation of the Schiff base ligands with metal (III) ions in 1:1 (L:M) mole ratio. Both the Schiff base ligands and their corresponding metal(III) complexes were characterized using various Physicochemical techniques such as solubility, conductivity, Melting point, FT-IR, UV/Vis,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, Microanalysis, Thermogravimetric analysis and differential Scanning Calorimetry (TGA/DSC), Powdered X-ray diffraction (PXRD), and *In Silico* molecular docking studies. The compounds obtained have various colors, with appreciable percentage yield ranging from (74 - 80%) was also obtained. The Schiff base ligands and their metal (III) complexes were solids with high melting points ranging between (192 - 248°C). Compounds were non-hygroscopic when exposed to air, indicating that they are stable under normal conditions. Conductivity test shows that the complexes are non-electrolytes, the molar conductance measurement values are  $6 \times 10^{-3} - 17 \times 10^{-3}$ . The FT-IR spectra of the complexes compared with that of the free ligands indicated coordination of the metal ion to the ligand through the nitrogen atom of the azomethine (HC=N) group and oxygen of the phenolic (-OH) group. The synthesized novel compounds were confirmed to have an octahedral geometry by the UV/Visible spectral data. The microanalysis result reveals that the ligands have a stoichiometry composition of 1:1 (aldehyde: Amine) and 1:1 mole ratio of metal to the ligand. Magnetic susceptibility analysis reveals that the complexes synthesized were paramagnetic. The Powdered X-ray diffraction revealed that the complexes of cobalt and iron are crystalline, while the complexes of chromium are amorphous. The Thermo-gravimetric and differential scanning calorimetry results reveal that there was loss of water molecules in all the complexes, in the first decomposition stage, where the second decomposition step represents the decomposition of the organic molecules (ligands). And the third and final decomposition step was for the metal oxides. NMR result confirmed the ligands and complexes formations. Molecular docking result of the study revealed that all the eight ligands formed stable conformation within the substrate binding site of the GS proteins and considered as suitable inhibitors of GS proteins after successful experimental validations.

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