

<https://africanjournalofbiomedicalresearch.com/index.php/AJBR>

*Afr. J. Biomed. Res. Vol. 28(2s) (February 2025); 1159-1175*

Research Article

# Sustainable N<sub>2</sub>O<sub>2</sub>S Azomethine Transition Metal Complexes: Synthesis, Characterization, and Bioactivity

Varsha D. Manvatkar<sup>1\*</sup>, Rajendra S. Dongre<sup>2</sup>, Sudhakar M. Bansod<sup>3</sup>

<sup>1</sup>\*PGTD Chemistry, R. T. M. Nagpur University, Nagpur, (M.S.)-440033, India. ORCID: 0000-0003-4583-0430

<sup>2</sup>G. D. M. Arts, K. R. N. Commerce & M. D. Science College, Jamner, Jalgaon (M.S.)-424206, India. ORCID:0000-0001-6607-5230

<sup>3</sup>CSIR-Indian Institute of Chemical Technology, Hyderabad, (TS)-500007, India.

**\*Correspondence Author:** Varsha D. Manvatkar

\*Email:varsha.manvatkar@gmail.com

## Abstract:

This study uses ultrasonication pathways to create a new and environmentally friendly condensation reaction method. These pathways involve o-vanillin and thiocarbohydrazide coming together in a 2:1 molar ratio. The ligand is named as (thalvan) (1E,5E)-1,5-bis(2-hydroxy-3-methoxybenzylidene)thiocarbonohydrazide. The thalvan ligand is soluble in aprotic polar solvent like DMSO, DMF, acetonitrile, and dichloromethane. The metal acetates (M(OAc)<sub>2</sub>, where M = Co(II), Ni(II), Cu(II), and Zn(II)), undergo ultrasonic reactions with the thalvan ligand to produce stable complexes. The ligands may include nitrogen, oxygen, and sulfur donor atoms. All complexes are synthesized in high yield by an equivalent ratio of the thalvan ligands with the corresponding metal salts. Spectral like Infrared (IR), UV-Vis, <sup>1</sup>H and <sup>13</sup>C NMR, Mass, elemental, ICPMS, magnetic susceptibility, and conductivity studies have been employed to characterize this thalvan ligand and its coordinated complexes. The antibacterial capabilities against bacterial species, specifically *Staphylococcus aureus* (gram-positive) and *Pseudomonas aeruginosa* (gram-negative), as well as the antioxidant activity assessed using H<sub>2</sub>O<sub>2</sub> and DPPH techniques, were evaluated for the azomethine thalvan ligand and their coordinated compounds.

**Keywords:** Azomethine, coordinated compounds, antimicrobial, antioxidant, sonochemical

\*Author for correspondence: Email: varsha.manvatkar@gmail.com

Received: 27/12/2024

Accepted: 25/01/2025

DOI: <https://doi.org/10.53555/AJBR.v28i2S.7013>

© 2025 The Author(s).

This article has been published under the terms of Creative Commons Attribution-Noncommercial 4.0 International License (CC BY-NC 4.0), which permits noncommercial unrestricted use, distribution, and reproduction in any medium, provided that the following statement is provided. "This article has been published in the African Journal of Biomedical Research"

## 1. Introduction

Green chemistry is being actively pursued by the international scientific community, which is defined by the search for methods that are remarkably efficient, environmentally sustainable, and economical. Azomethine metal coordinated compounds are a significant area of research within this paradigm[1]. Azomethine ligands have existed since 1864, when

German scientist "Hugo Schiff" first reported how primary amines combine with carbonyl moiety to produce imines[2]. These substances are now referred to as Schiff bases and bear Hugo Schiff's name. Metal complexes (MCs), also known as Schiff base coordination, exhibit a significant character in a variety of domains. The applications of azomethine ligand and

their MCs are therefore numerous and include biological, medical, analytical, catalytic, and industrial[3]. SBLs have uses in anticancer, antioxidant, antibacterial[4], insecticidal, and plant growth regulation within the agricultural sector[5]. Schiff base complexes possess significant utility in various domains, including catalysis, optical devices[6], dyes[7], medicines[8], and nanotechnology[9]. SBL, when complex with copper metal, exhibits anti-cancer effects[10]. Contemporary research and development are persistently exploring novel applications for Schiff bases. They constitute a diverse category of chemicals, possessing numerous potential applications. Owing to the considerable applicability of azomethine coordinated compounds across diverse domains, researchers have devised multiple methodologies for their production. Numerous techniques, including traditional, microwave-assisted[11], ultrasonication[12], natural acid-catalyzed synthesis[13], etc., have been used to synthesize the MCs of imine ligands[14].

Inorganic chemists are interested in chelating agents with O, N, and S donor atoms because they have a wide spectrum of biological activity and can attach to metal ions in various ways[15]. Biologists synthesize biologically active metal chelates and other biological applications using Schiff bases with ONS donor

atoms[16]. Researchers extensively study Schiff base transition metal chelates for their industrial, antifungal, and antibacterial properties, as well as their biological applications. Scientists know that Schiff bases, which include ONS donor atoms, can make stable chelates because of their denticity[17]. These stable chelates exhibit enhanced solubility and bioavailability, making them valuable in various therapeutic contexts. Schiff base transition metal complexes are also reactive and have the potential to speed up chemical reactions because of the way their structures are made[18]. These atoms are present in chelates, rendering these compounds stereospecific catalysts for redox[19], and various other chemical reactions in both organic and inorganic chemistry. There are medicines that work better as metal chelates than as their free ligand forms[20]. The present investigation explores the ultrasonic pathway of synthesis and examination of the azomethine ligand (thalvan) (1E,5E)-1,5-bis(2-hydroxy-3-methoxybenzylidene)thiocarbonohydrazide and their coordinated complexes formed using Co(II), Ni(II), Cu(II), and Zn(II) metal ions, elucidating their potential applications in biological activity. Based on spectral, physical, and analytical evidence, metal chelates' structural properties have been proposed. The thalvan azomethine ligand utilized in this investigation is depicted as follows in Figure 1.

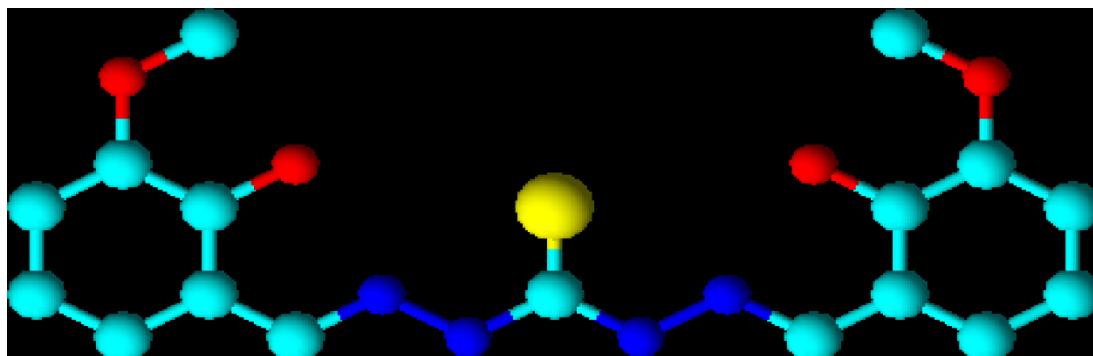


Figure 1: 3D structure of thalvan ligand.

## 2. Experimental methods

### 2.1. Materials and Apparatus

All commercial-grade materials are utilized. The open capillary approach determined all uncorrected melting points. TLC evaluated the synthesis of the azomethine ligand and metal coordinated compounds, and UV radiation exposed the spots. UV-Vis 1800 Shimadzu Spectrophotometers recorded absorbance spectra[21]. We obtained the FTIR (wavenumber in cm<sup>-1</sup>) and <sup>1</sup>H and <sup>13</sup>C NMR spectra of the ligand on a model Avance-II (Bruker), using CDCl<sub>3</sub> solution and tetramethylsilane as chemical shift reference. LC-MS with electrospray ionization and the Waters Micromass Q-ToF micro[22] high-resolution were used to record the mass spectra. The compound's C, H, and N elements were analysed using the Elementar Vario EL III elemental analyser. The results were in excellent alignment with the calculated values. The "Spectralab model 40D Ultrasonic cleaner" with a powerful transducer at 40 KHz and 250W power is used for ultrasonic-assisted reactions. The reaction

flask was held in the middle of the ultrasonication bath. A heating adjustment controlled the reaction temperature.

### 2.2. Synthesis of ligand 'L':

According to the study, traditional techniques for creating Schiff bases include the use of organic solvents and lengthy reaction times. We provide a new, eco-friendly condensation reaction technique using ultrasonication channels to condense o-vanillin with thiocarbonohydrazide. To the solution of (2 mmol) 2-hydroxy-3-methoxybenzaldehyde in 5 ml of ethanol with glacial acetic acid and sonicated for 2 mins. To this solution, 1mmol of thiocarbonohydrazide in 5 ml ethanol was added dropwise and further sonicated for 2 hours. The precipitate was separated with filtration, washed thrice with a 60% alcoholic solution, and then recrystallized. TLC, using chloroform and pet ether as the mobile phase, determined the product's purity. The obtained product was soluble in polar aprotic solvents.

Table 1 represented the physical and analytical statistics of the thalvan ligand.

**Table 1: Physical and analytical data of the azomethine ligand (thalvan).**

| Compound  | Yield (%) | Colour        | Melting point (°C) | Solubility                 | Chemical Composition<br>(C <sub>17</sub> H <sub>18</sub> N <sub>4</sub> O <sub>4</sub> S)<br>(Detected %) |      |       |       |
|---|-----------|---------------|--------------------|----------------------------|---|------|-------|-------|
|   |           |               |                    |                            | C   | H    | N     | S     |
| Ligand-<br>Thalvan<br>(C <sub>17</sub> H <sub>18</sub> N <sub>4</sub> O <sub>4</sub> S) | 86.70     | Pale<br>peach | 218                | DMSO, DMF,<br>Acetonitrile | 49.76   | 5.04 | 12.87 | 10.25 |

The ligand is multidentate with N<sub>2</sub>O<sub>2</sub>S donor atoms. The ligand had the ability to form a stable coordinate complex with metal (II) acetates M(OAc)<sub>2</sub>, where M = (Co, Ni, Cu, and Zn), resulting in stable coordinated compounds. A 1:1 molar reaction between the imine ligand and the accompanying metal acetates forms all the complexes in high yield. To describe the ligand and their complexes, we used infrared (IR), <sup>1</sup>H and <sup>13</sup>C NMR, spectrophotometry, and chemical composition analysis. At length, we assess the antimicrobial, and antioxidant action of the synthesized donor molecule and metal coordinated complexes[23].

### 2.3. A general method for the complexation of N<sub>2</sub>O<sub>2</sub>S ligand

The coordinated materials were obtained by drop-wise[24] count of alcoholic solutions of cobalt, nickel, copper, and zinc salts (1 mmol) to azomethineN<sub>2</sub>O<sub>2</sub>ligand (1 mmol) while mixing steadily. TLC evaluated the reaction mixture after 3 hours of sonication. After centrifugation, we washed the precipitate with ethanol and water and vacuum-dried it. Table 2, describe the physical data of the metal coordinated complexes.

**Table 2: The physical data of coordinated metal complexes of thalvan ligand.**

| S. No. | Compounds                        | Yield | Color  | M. Pt. (°C) |
|--------|----------------------------------|-------|--------|-------------|
| 1.     | [Co(thalvan)]                    | 81.3  | Orange | >300        |
| 2.     | [Ni(thalvan)](AcO <sup>-</sup> ) | 75.4  | Green  | 280         |
| 3.     | [Cu(thalvan)](AcO <sup>-</sup> ) | 76.8  | Black  | >300        |
| 4.     | [Zn(thalvan)]                    | 79.6  | Yellow | 210         |

### Biological applications of Schiff bases

The large numerous lives threaten by microorganism include micro bacteria and virus which is increasing their Empire Day to day in worldwide. Coordination as ligands with metal ions enhances the biological and therapeutic effect. Derivatives of Schiff bases are noteworthy due to their diverse biological applications. Schiff bases include the -N=CH- (imine) moiety, which is important for the various biochemical reactions occurring in the entire biological ecosystems. These findings prompted and applied in society to us to investigate the biological importance of azomethine ligands and their Co(II), Ni(II), Cu(II), and Zn(II) coordinated compounds have been studied for their bactericidal assay against the *Streptomyces aureus* as monoderm bacterial strain and diderm *Pseudomonas fluorescens* bacterial strain. The streptomycin drug is used as the standard to compare the antimicrobial activity. The DPPH assay and the H<sub>2</sub>O<sub>2</sub> scavenging assay were used to test the antioxidant nature of Co(II), Ni(II), Cu(II), and Zn(II) compounds of the azomethine ligands. Also, the butylated hydroxytoluene (BHT) was used as a standard to compare the in vitro antioxidant effect with ascorbic acid (AA).

#### 3.1. Antibacterial assay procedure

The azomethine ligand and its Co(II), Ni(II), Cu(II), and Zn(II) coordinated compounds were produced and tested against two types of microbial culture strains. The primary objective of this investigation is to find an

antibacterial substance that can kill pathogenic germs effectively without hurting patients.

Using the disc diffusion method[25], the Co(II), Ni(II), Cu(II), and Zn(II) coordinated molecules were tested in a test tube contrary to *Streptomyces aureus* (monoderm) and *Pseudomonas aeruginosa* (diderm). They were also tested with their parent Schiff base ligand. We used a concentration of 100 g/ml. Sterilized growth agar media was poured into a sterile culture plate and kept for 24 hours to allow solidifying at room temperature and to ensure proper sterilization. Using a spreader of 0.1 ml of the given test bacterial suspension over the culture plate after it solidified. In the above concentrations, test ligands and their complex solutions were put on 5 mm Whatman No. 1 filter paper discs of different sizes. The discs were placed four times as far apart in the inoculated Petri plates.

In this experiment, streptomycin was used as the reference drug and prepared control discs on filter paper using DMF. The culture plates were kept at a temperature of 37 °C for a duration of one day. Each compound was tested in triplicate, and the average measurements for each were documented.

#### 3.2. Antioxidant activity

##### 3.2.1. The DPPH free radical quenching assay

The measurement of 2,2-Diphenyl-1-picryl-hydrazyl (DPPH) antioxidant assay is a crucial and standardized technique for assessing antioxidant activity. The assessment of the antioxidant assay of azomethine

compounds and their coordinated complexes was conducted using the DPPH technique[26], [27]. In this method, a decrease in the DPPH solution's absorbance indicates the tested compounds' ability to donate electrons and neutralize free radicals. The absorbance values before and after adding the samples can help researchers determine the scavenging capacity and health benefits of these compounds. When DPPH radicals combine with existing reducing agents, they pair electrons with the corresponding hydrazine. The Schiff base compounds and their complex solutions that were looked at lost color depending on how many electrons they took in and what substances could donate electrons or hydrogen atoms. The Schiff base compounds under examination were synthesized in DMSO. A 1 mL aliquot of the solution,

with a concentration of 100 µg/ml, was added in the test tube, with 4 mL of a 0.1 mM methanolic DPPH solution, which was agitated continuously until a clear solution was obtained. The test tubes were thereafter incubated in darkness for half an hour. The measurement of absorbance at a wavelength of 517 nm was carried out using a spectrophotometer. This device allowed for precise analysis of the sample's light absorption at that specific wavelength. Ascorbic acid served as the reference standard[28]. The antioxidant assay was performed in triplicate, and the percentage was determined using the subsequent formula:

Where, A<sub>0</sub> represents the optical density of the blank (without compound)

A<sub>1</sub> is the optical density of the Schiff base moiety.

$$\text{DPPH scavenging activity (\%)} = \left[ \frac{A_0 - A_1}{A_0} \times 100 \right]$$

### 3.2.2. Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) radical scavenging activity

As shown in the method[29], the Schiff base compounds and their complexes that were made could get rid of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>). The experiments on Schiff base compounds were performed in triplicate, and the average means were documented. The Fenton reaction created hydroxyl radical ions in the aqueous medium. The assay comprised 2.5 ml of phosphate buffer (0.15 M, pH 7.4), 0.5 ml of 114 µM safranin, 1 ml of 945 µM EDTA-Fe(II), 1 ml of 3% H<sub>2</sub>O<sub>2</sub>, and 100 µg/mL of the Schiff base compound solution produced in DMSO.

Once the solution reached the desired consistency, we began the process of carefully transferring it into labeled containers for further analysis. This step was crucial to ensure accurate results in our subsequent experiments. The blank reaction mixture was taken as

the control. The investigated synthetic fusions were heated up at 37°C for 1 hour in a water bath[30]. After the sterilization period, the samples were carefully analyzed for any observable changes or reactions. The results were then recorded and analyzed to determine the effectiveness of the test compound compared to the control. The optical density of the tested mixture ere measured at 520 nm wavelength. The following formula was applied for the calculation of Scavenging ratio. This calculation facilitates the evaluation of the antioxidative potential of the compounds under investigation.

Where, A<sub>i</sub> indicates the optical density of the tested compound in the reaction mixture. A<sub>o</sub> represents the optical density of a compound that has undergone absence testing. A<sub>c</sub> represents the optical density of blank, containing EDTA-Fe (II), and H<sub>2</sub>O<sub>2</sub> solutions[28].

$$\text{Scavenging ratio (\%)} = \left[ \frac{A_i - A_o}{A_c - A_o} \times 100 \right]$$

## 4. Results and Discussion

The 2-hydroxy-3-methoxybenzaldehyde was sonicated with thiocarbohydrazide in an ethanolic solution in a 2:1 M ratio to create the N<sub>2</sub>O<sub>2</sub>S donor symmetrical Schiff base. The ligand was further sonicated with an equal quantity of metal acetate in the ethanolic solvent in a 1:1 M ratio to create the [Co(thalvan)],

[Ni(thalvan)], [Cu(thalvan)], and [Zn(thalvan)] complexes Figure 2. In polar aprotic liquids, all of the chemical's dissolve. The suggested structure of the complexes is in excellent agreement with the spectrum investigations. Table 3 represents the spectroscopic data of thalvan ligand.

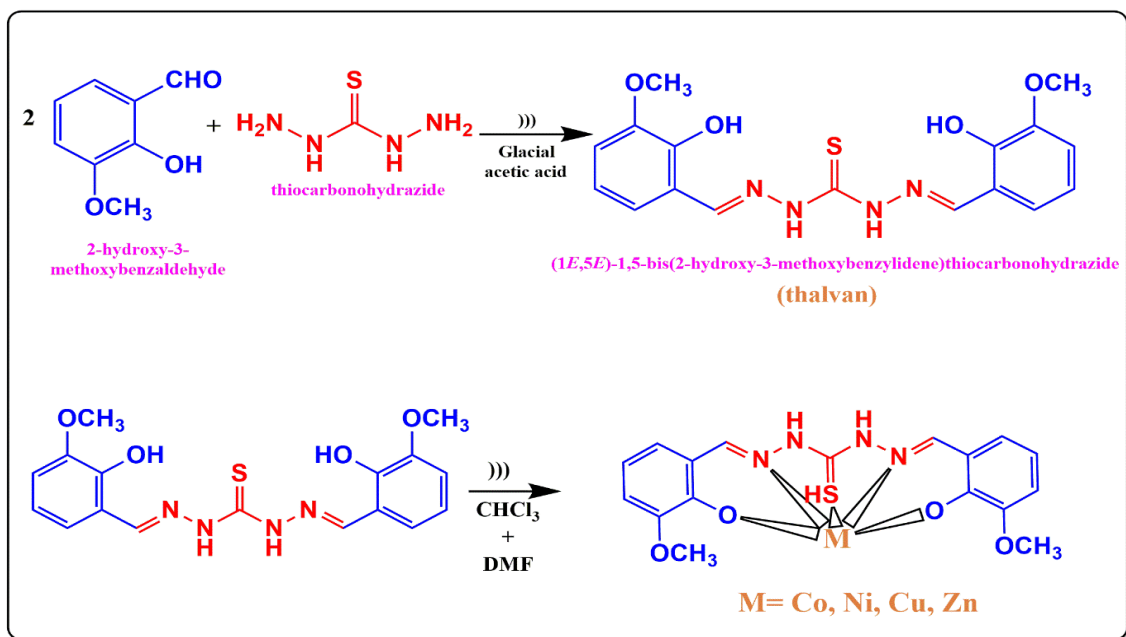


Figure 2: Green synthetic route for thalvan ligand and its coordinated complexes.

Table 3: The spectroscopic data of azomethine thalvan ligand.

| Compound   | UV<br>$\lambda$ max<br>(nm)                | FTIR<br>$\nu_{\max}$ in $\text{cm}^{-1}$                                      | NMR  |  | MASS<br>LCMS (TOF<br>MS ES+) for<br>$\text{C}_{17}\text{H}_{18}\text{N}_4\text{O}_4\text{S}$<br>(m/z) |
|--|--|---|--|--|---|
|  |  |   | <sup>1</sup> H NMR (500 MHz, CDCl <sub>3</sub> , TMS, $\delta$ , ppm, s= singlet, m=multiplet, q= quartet)                                       | <sup>13</sup> C NMR (500 MHz, CDCl <sub>3</sub> )                                      |   |
| Thalvan<br>(C <sub>17</sub> H <sub>18</sub> N <sub>4</sub> O <sub>4</sub> S) | 330 $\pi$ - $\pi^*$ ,<br>466 $n$ - $\pi^*$ | 3412 (-OH),<br>3284 (-NH),<br>1617 (-C=N),<br>1521823 (-C=S),<br>1252 (-C-O). | 12.06, 11.96 (s, 2H, -OH phenolic), 11.50, 9.82 (s, 2H, -NH), 9.5-9.7 (s, 2H, -CH=N), 6.94-7.95 (6H, m, Ar-H), 3.82 (6H, s, -OCH <sub>3</sub> ), | 39.91-55.94 (-OCH <sub>3</sub> ),<br>118.94 (Ar C-H),<br>147.96 (C=N),<br>174.33 (C=S) | [M+1] <sup>+</sup> =375;<br>[M-1] <sup>+</sup> =373   |

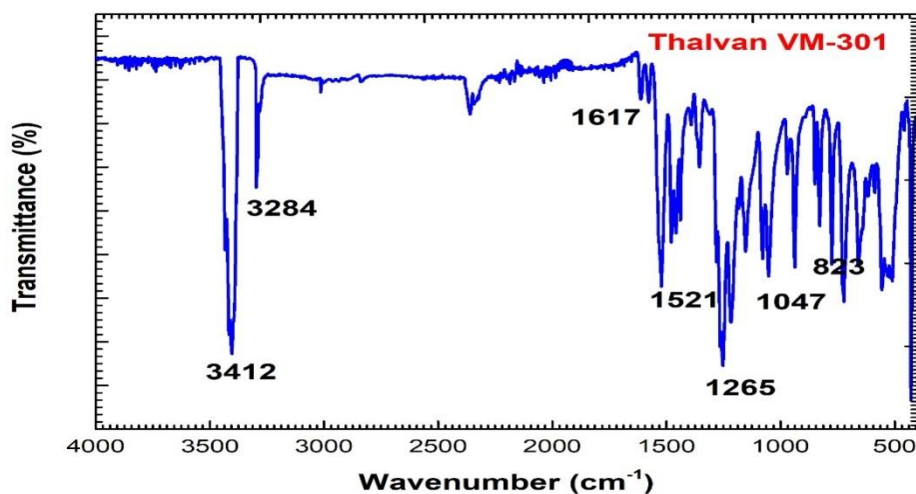


Figure 3: The FTIR Spectrum of thalvan ligand

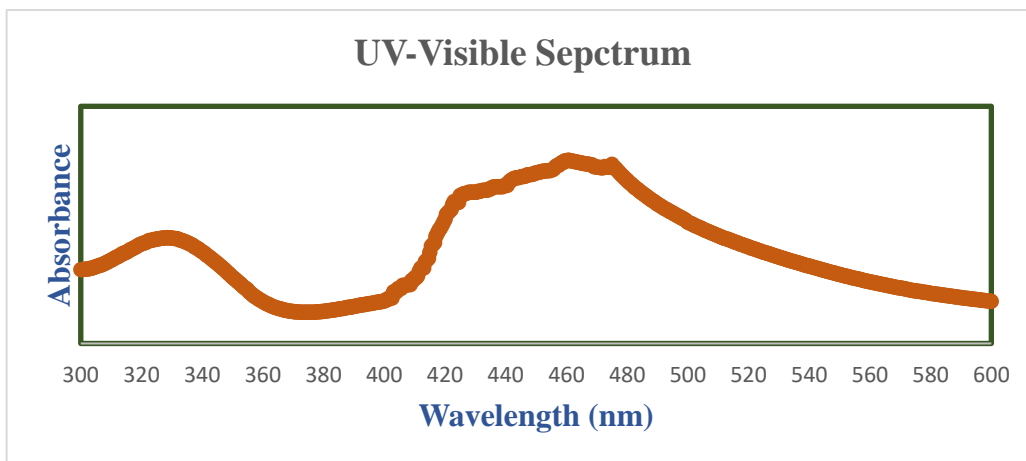


Figure 4: The UV-Vis spectrum of thalvan ligand.

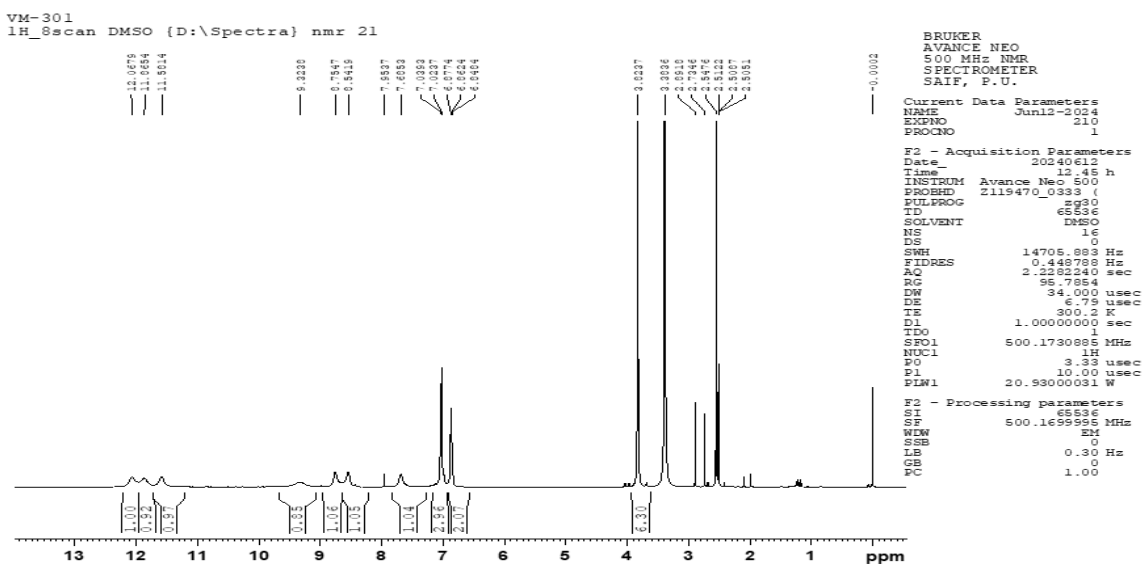


Figure 5: The <sup>1</sup>H NMR Spectrum of thalvan ligand.

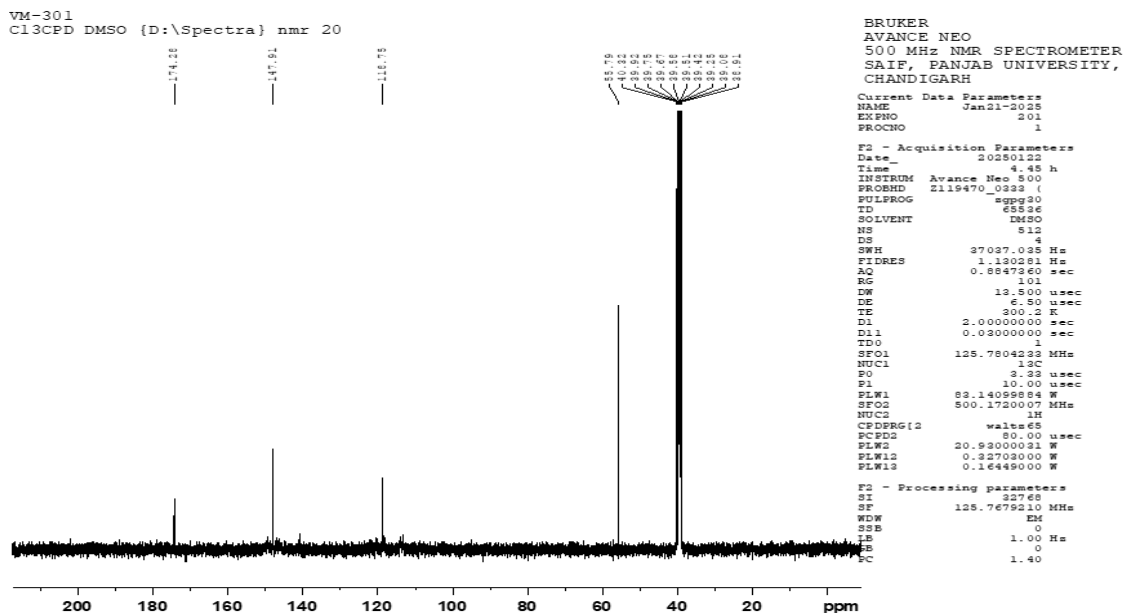


Figure 6: The <sup>13</sup>C NMR Spectrum of thalvan ligand.

#### 4.1. Spectral characterization

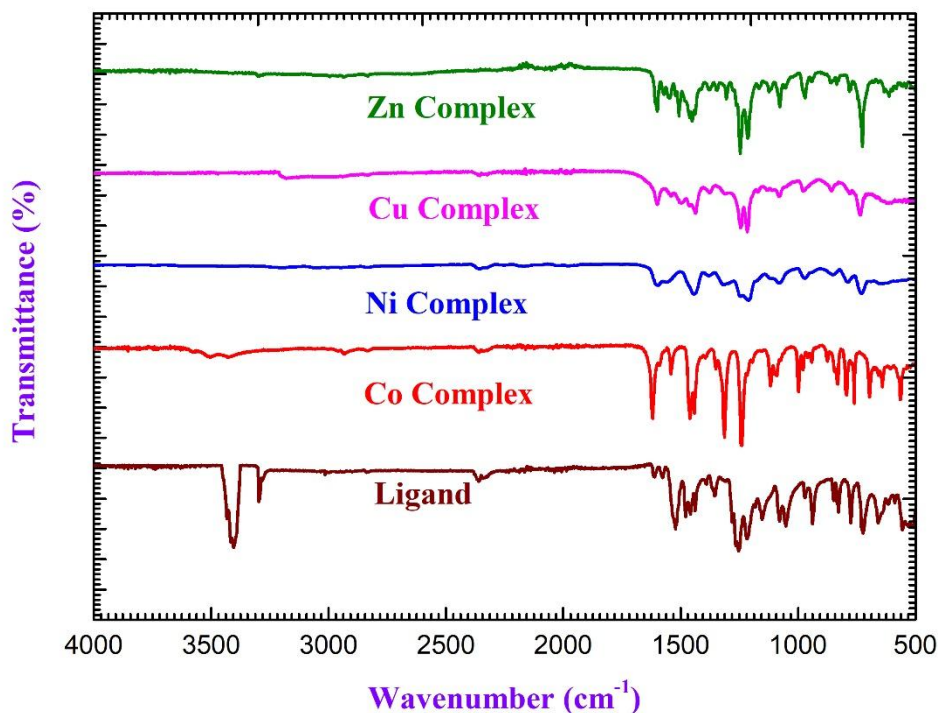
##### 4.1.1. IR spectrum

Table 4 displays the significant IR bands of the thalvan ligand and its coordinated compounds. The FTIR spectra of the uncoordinated ligand display a peak at 3412 cm<sup>-1</sup>, attributable to -OH (phenolic) stretching, which is absent in all four complexes. Additionally, the  $\nu(\text{C-O})$  stretching vibration is detected at 1252 cm<sup>-1</sup> in the unbound azomethine ligand. The energy is reduced to the range of 1210 cm<sup>-1</sup> to 1217 cm<sup>-1</sup>, showing coordination between the metal and the oxygen atom. This is additionally validated by the band detected in the chelates within the range of 484 cm<sup>-1</sup> to 453 cm<sup>-1</sup>, attributed to the  $\nu(\text{M-O})$  frequency. The band that

appears at 1617 cm<sup>-1</sup> in the imine ligand corresponds to the  $\nu(\text{C=N})$  stretching vibration. These lower frequency bands in metal chelates, which range from 12 cm<sup>-1</sup> to 19 cm<sup>-1</sup>, indicate that the imine nitrogen is coordinated with the core metal atom. Metal chelates assigned to the  $\nu(\text{M-N})$  frequency display a band in the region of 611 cm<sup>-1</sup> to 729 cm<sup>-1</sup>, which further supports the coordination between the metal atom and nitrogen. The FTIR spectra of the ligand molecules displays bands at 1521 cm<sup>-1</sup> and 823 cm<sup>-1</sup>, attributed to  $\nu(\text{C=S})$  and  $\delta(\text{C=S})$ , respectively. These bands change to lower wave numbers by 60 cm<sup>-1</sup> to 80 cm<sup>-1</sup> in metal chelates, showing the coordination of sulfur to the metal centre. The  $\nu(\text{-NH-})$  stretch is assigned to the single band that was seen between 3128 and 3284 cm<sup>-1</sup>.

**Table 4: IR spectrum data for thalvan and its coordinated compounds.**

| Compounds                                       | $\nu(\text{OH})$ | $\nu(\text{-NH})$ | $\nu(\text{C=N})$ | $\nu(\text{C=S})$ | $\nu(\text{C-O})$ | $\nu(\text{M-N})$ | $\nu(\text{M-O})$ |
|---|------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Thalvan   | 3412             | 3284              | 1617              | 1521, 823         | 1252              | ---               | ---               |
| Co-thalvan                                      | ---              | 3208              | 1605              | 1459, 845         | 1215              | 623               | 453               |
| Ni-thalvan. (CH <sub>3</sub> COO <sup>-</sup> ) | ---              | 3184              | 1598              | 1444, 851         | 1210              | 729               | 456               |
| Cu-thalvan. (CH <sub>3</sub> COO <sup>-</sup> ) | ---              | 3128              | 1599              | 1436, 857         | 1216              | 726               | 484               |
| Zn-thalvan                                      | ---              | 3198              | 1599              | 1436, 835         | 1213              | 611               | 466               |



**Figure 7: FTIR spectrum of thalvan ligand and their coordinated complexes.**

##### 4.1.2. Mass spectrum

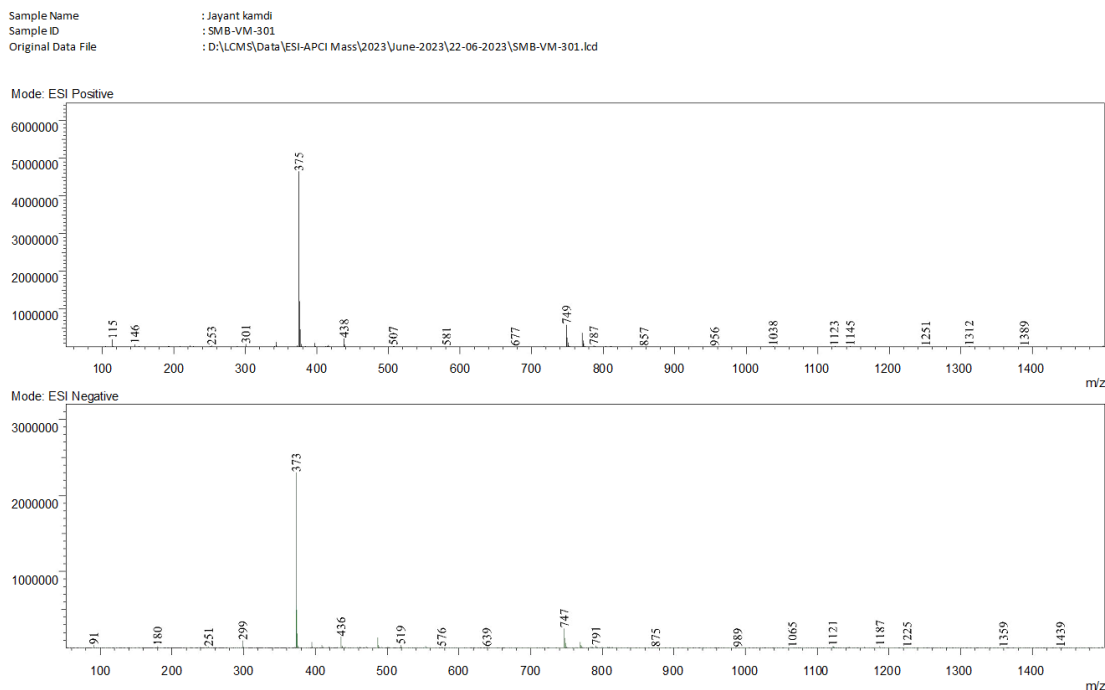
The mass spectrum of azomethine thalvan ligand [C<sub>17</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub>S] in the current study reveals a M<sup>+</sup> ion peak at m/z = 375 corresponds to [M+1]<sup>+</sup> peak and m/z = 373 resembles to [M-1]<sup>-</sup> peak. The spectrum of [Co(thalvan)] complex show [M+1]<sup>+</sup> and [M-1]<sup>-</sup> ion at m/z 432 and 433 respectively with a molecular ion peaks at m/z = 431. The spectra of

[Ni(thalvan)](CH<sub>3</sub>CO) complex show [M+1]<sup>+</sup> and [M-1]<sup>-</sup> ion at m/z 472 and 474 respectively with a molecular ion peaks at m/z = 473. The spectra of [Cu(thalvan)](CH<sub>3</sub>CO) complex show [M+1]<sup>+</sup> and [M-1]<sup>-</sup> ion at m/z 478 and 480 respectively with a molecular ion peaks at m/z = 479. The spectra of [Zn(thalvan)] complex show [M+1]<sup>+</sup> and [M-1]<sup>-</sup> ion at m/z 438 and 436 respectively with a molecular ion

peaks at m/z =437. The stoichiometry of the complexes' [ML] is confirmed by the m/z of all azomethine ligand fragments and their coordinated

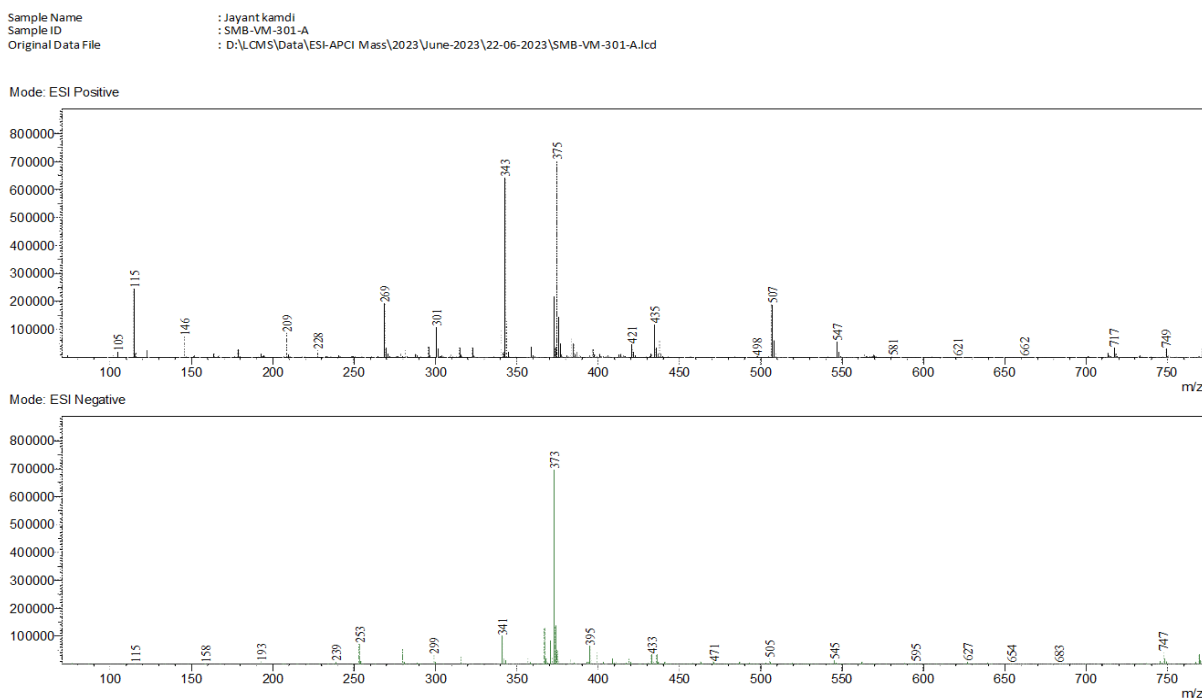
complexes. In **Figure 8 (a-e)**, the mass spectrum of the ligand and their coordinated compounds is illustrated.

=== FAC DIVISION @ CSIR-IICT ===



(a)

=== FAC DIVISION @ CSIR-IICT ===

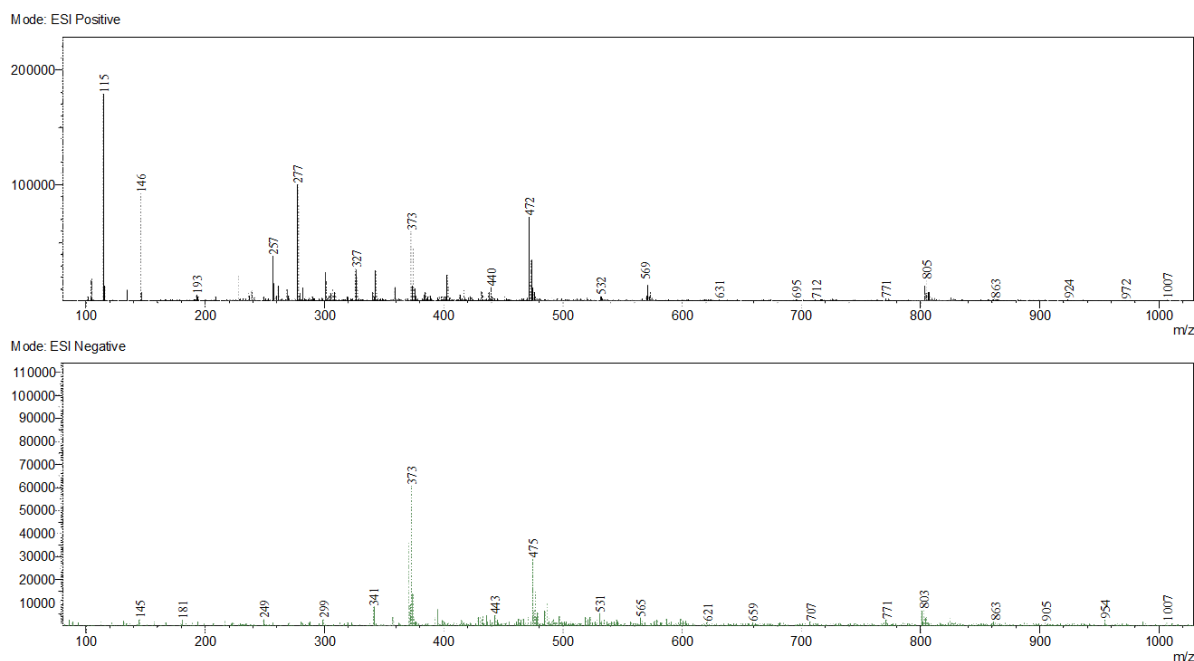


(b)



=== FAC DIVISION @ CSIR-IICT ===

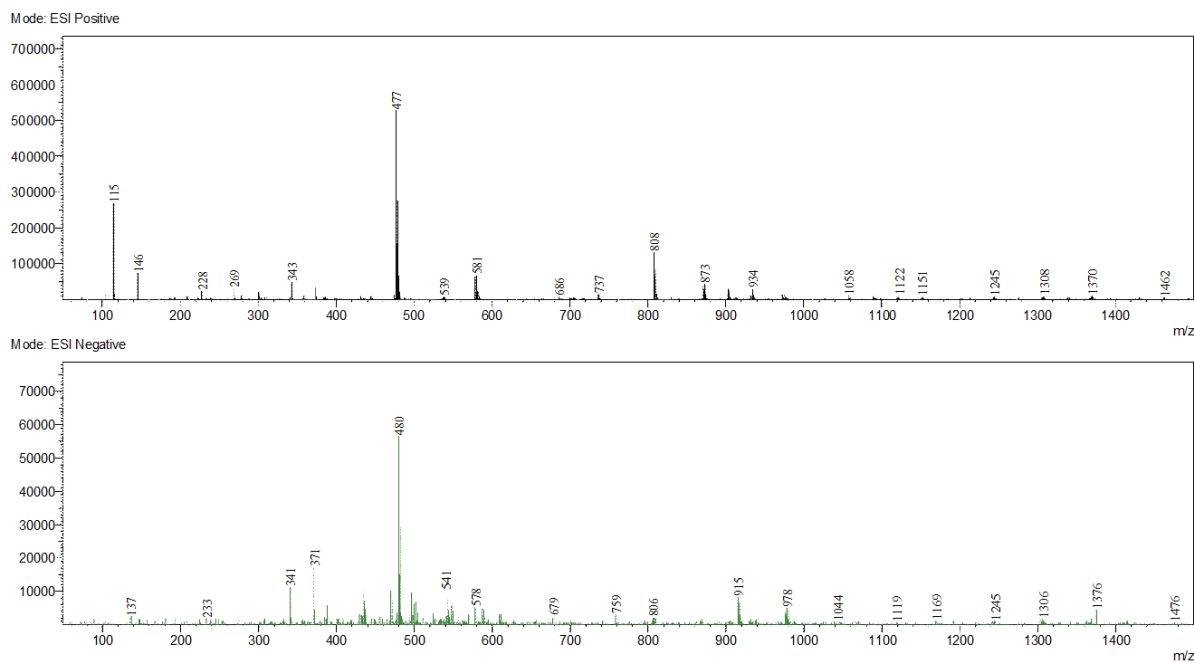
Sample Name : Jayant kamdi  
Sample ID : SMB-VM-301-B  
Original Data File : D:\LCMS\Data\ESI-APCI\_Mass\2023\June-2023\22-06-2023\SMB-VM-301-B\cd



©

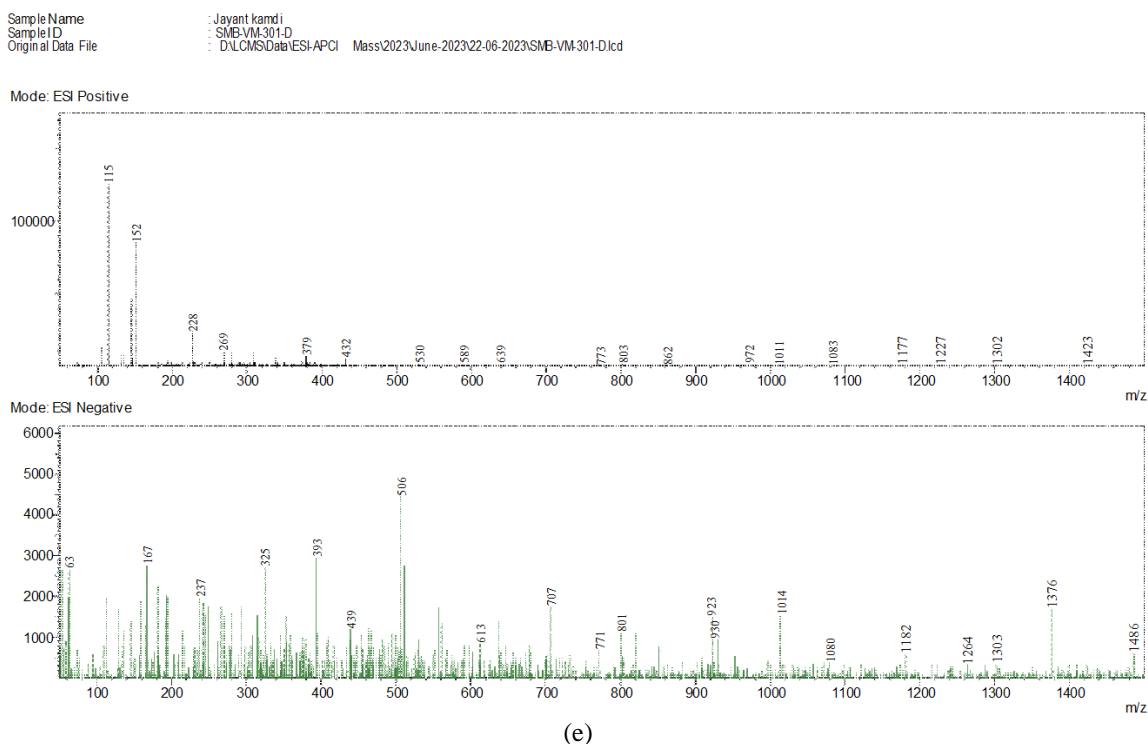
=== FAC DIVISION @ CSIR-IICT ===

Sample Name : Jayant kamdi  
Sample ID : SMB-VM-301-C  
Original Data File : D:\LCMS\Data\ESI-APCI\_Mass\2023\June-2023\22-06-2023\SMB-VM-301-C\cd



(d)

=== FAC DIVISION @ CSIR-IICST ===



**Figure 8.** The mass spectrum of (a) the thalvan ligand (b) [Co(thalvan)] (c) [Ni(thalvan)]. AcO<sup>-</sup> (d) Cu(thalvan)]. AcO<sup>-</sup> (e) [Zn(thalvan)] coordinated compounds.

#### 4.1.4. ICPMS and Elemental analysis

Inductively Coupled Plasma Mass Spectrometry (ICP-MS) and elemental data are the two key analytical techniques used to characterize ligands and their metal-coordinated complexes. ICP-MS is used to detect and quantify the presence of metals in a sample with high sensitivity and precision. The sample is dissolved

using acid digestion for solid complexes. The elemental analysis technique confirms the ligand composition after coordination with the metals. **Table 5**, below show the metal complex composition as determined by elemental analysis and ICPMS.

**Table 5: Elemental and ICPMS data of thalvan coordinated compounds.**

| S. No. | Compounds                        | Elemental Analysis    |             |               |             | ICP-MS Analysis |       |      |       |
|--------|----------------------------------|-----------------------|-------------|---------------|-------------|-----------------|-------|------|-------|
|        |                                  | Calculated (observed) |             |               |             | Co              | Ni    | Cu   | Zn    |
|        |                                  | C                     | H           | N             | S           |                 |       |      |       |
| 1.     | [Co(thalvan)]                    | 47.34 (42.27)         | 3.71 (3.96) | 12.99 (11.15) | 7.4 (6.46)  | 5.20            | -     | -    | -     |
| 2.     | [Ni(thalvan)](AcO <sup>-</sup> ) | 46.55 (42.19)         | 3.87 (3.89) | 11.43 (11.66) | 6.53 (6.11) | -               | 4.469 | -    | -     |
| 3.     | [Cu(thalvan)](AcO <sup>-</sup> ) | 43.31 (43.41)         | 4.24 (3.60) | 11.88 (11.39) | 6.79 (6.85) | -               | -     | 2.81 | -     |
| 4.     | [Zn(thalvan)]                    | 46.68 (39.01)         | 3.66 (3.67) | 12.81 (10.75) | 7.3 (5.93)  | -               | -     | -    | 10.44 |

#### 4.1.5. Measurement of conductivity

The molar conductivities of the complexes with a concentration of 10<sup>-3</sup> M solutions were determined at ambient temperature. The complexes exhibited molar conductivity values ranging from 2.5 to 5.0  $\Lambda\text{m}\ \Omega^{-1}\ \text{cm}^2\ \text{mol}^{-1}$ . The range of conductivity values suggests that the coordinated compounds are non-conductive in nature.

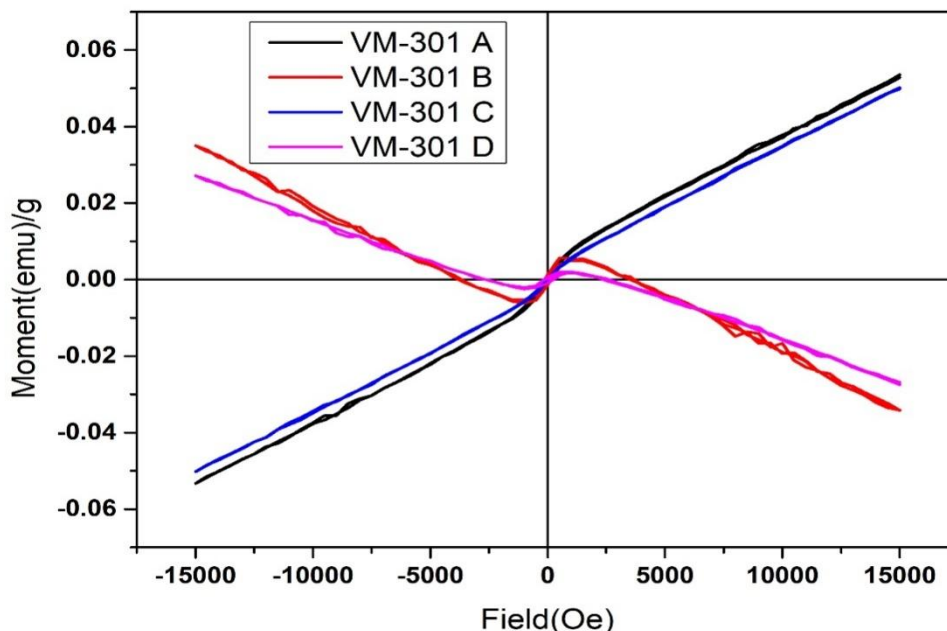
#### 4.1.6. Magnetic susceptibility

The magnetic moment of the compounds is determined by a Vibrating Sample Magnetometer (VSM). The

[Co(thalvan)] compound shows the paramagnetic moment 1.92 B M., which matches for Co(II) d<sup>7</sup> configuration with dsp<sup>3</sup> hybridization, corresponding to trigonal bipyramidal geometry, typically resulting in a low-spin configuration due to the strong ligand field of the N<sub>2</sub>O<sub>2</sub>S ligand. The trigonal bipyramidal geometry and diamagnetic nature characterize the [Ni(thalvan)].(CH<sub>3</sub>COO<sup>-</sup>) complex. The [Cu(thalvan)].(CH<sub>3</sub>COO<sup>-</sup>) complex is trigonal bipyramidal geometry and paramagnetic in nature, with a magnetic moment of 1.059 BM. The [Zn(thalvan)] complex shows trigonal bipyramidal geometry with

sp<sup>3</sup>d hybridization and diamagnetic nature. **Figure 9** displays the VSM spectrum of metal complexes containing the azomethine ligand. Table 6 display the

spectral and analytical data of thalvan ligand and its coordinated compounds.



**Figure 9:** VSM spectrum of metal complexes of thalvan ligand.

**Table 6:** The mass, magnetic and conductivity measurement of thalvan ligand and its coordinated complexes.

| S. No. | Compounds                        | Molecular formula  | MASS LCMS (TOF MS ES+)                              | Vibrating Sample Magnetometer $\mu_{\text{eff}}$ (B M) | Geometry of the complexes                | Conductivity Measurement (in DMF) [ $\Lambda_m = \Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$ ] |
|--------|----------------------------------|--|---|--|--|---|
| 1.     | [Co(thalvan)]                    | [C <sub>17</sub> H <sub>16</sub> N <sub>4</sub> O <sub>4</sub> SCo]                                    | [M+1] <sup>+</sup> =432;<br>[M-1] <sup>+</sup> =430 | 1.92   | Trigonal bipyramidal (dsp <sup>3</sup> ) | 2.913   |
| 2.     | [Ni(thalvan)](AcO <sup>-</sup> ) | [C <sub>17</sub> H <sub>16</sub> N <sub>4</sub> O <sub>4</sub> SNi](CH <sub>3</sub> COO <sup>-</sup> ) | [M+1] <sup>+</sup> =474;<br>[M-1] <sup>+</sup> =472 | 0.481  | Trigonal bipyramidal (dsp <sup>3</sup> ) | 2.591   |
| 3.     | [Cu(thalvan)](AcO <sup>-</sup> ) | [C <sub>17</sub> H <sub>16</sub> N <sub>4</sub> O <sub>4</sub> SCu](CH <sub>3</sub> COO <sup>-</sup> ) | [M+1] <sup>+</sup> =478;<br>[M-1] <sup>+</sup> =480 | 1.868  | Trigonal bipyramidal (sp <sup>3</sup> d) | 4.488   |
| 4.     | [Zn(thalvan)]                    | [C <sub>17</sub> H <sub>16</sub> N <sub>4</sub> O <sub>4</sub> SZn]                                    | [M+1] <sup>+</sup> =438;<br>[M-1] <sup>+</sup> =436 | 0.416  | Trigonal bipyramidal (sp <sup>3</sup> d) | 4.464   |

## 5. Biological studies of thalvan ligand and its metal coordinated compounds.

### 5.1. Antibacterial activity

The bactericidal efficacy of azomethine ligands and their Co(II), Ni(II), Cu(II), and Zn(II) compounds was evaluated contrary to the monoderm bacterium *Streptomyces aureus* and the diderm bacterium *Pseudomonas aeruginosa*. The antibacterial activity inhibition data are compared with the conventional antibacterial agent, streptomycin. It is clear that the complexes show significant activity against *Streptomyces aureus* and *Pseudomonas aeruginosa*. This is possible due to the -NH, -C=N and -OH group presence into the organic ligand plays a significant role in the antibacterial assay which is responsible for

exhibit significant activity. These -NH and -C=N group in the organic ligand are conveyed the transformations in cellular morphology[31]. The ligands are very important in the antibacterial test because they have a big effect on how well the antibiotic compounds bind and work. Understanding the interactions between the ligand and bacterial targets is crucial for developing more effective treatments[32], [33].

The results on the antibacterial activity of synthesized azomethine ligands and their coordinated molecules are presented in Table 7. The resulting statistics shows that, the synthesized complexes were found to be more effective and improve antibacterial activity as compared with their parent free ligand but less as compared with standard beneath the replication of

circumstances. The enhancement of antibacterial activity in the coordinated complexes is attributable to the impact of the central metal cation on normal cellular processes. The evaluated Co(II), Ni(II), Cu(II), and Zn(II) compounds significant activity against monoderm bacteria compared to diderm bacteria, signifying that the antibacterial efficacy of the complexes is associated with the structural arrangement of the bacterial cell membrane[34].

Monoderm bacteria possess a thick cellular structure composed of numerous sheets of teichoic acids and peptidoglycan, whereas diderm bacteria have a thin cell wall consisting of a limited number of peptidoglycan

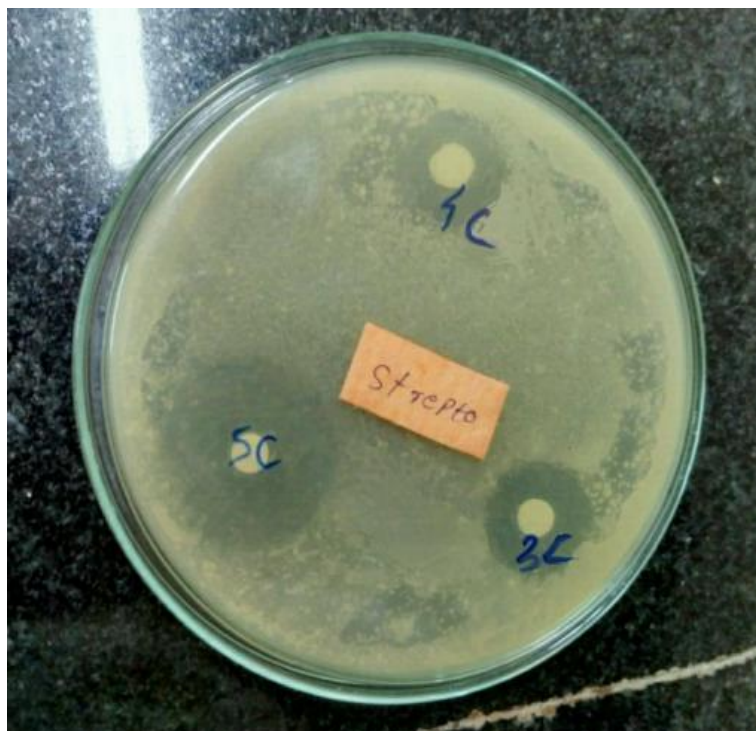
layers, encased by an additional triglycerides membrane that contains lipopolysaccharides and lipoproteins. The difference in cellular wall composition can result in differing bactericidal susceptibility, with certain antibiotics capable of exclusively targeting Gram-positive bacteria, in contrast to Gram-negative bacteria[35].

The antimicrobial activity resulting data shows that the complexation with Co(II) and Cu(II) ion enhances activity of the azomethine ligands. Mainly Cu(II) complexes show effective antibacterial activity as compared to their thalvan ligand. Figure 10, show the zone of inhibition of antibacterial activity.

**Table 7: Antibacterial activity data of thalvan ligand and their coordinated compounds.**

| Compounds                        | Ref. On Disk | Zone of inhibition (mm)              |   |
|----------------------------------|--------------|--------------------------------------|---|
|                                  |              | <i>Streptomyces aureus</i> (Gram+ve) | <i>Pseudomonas aeruginosa</i> (Gram-ve) |
| Thalvan ligand                   | 1L           | -ve                                  | -ve                                     |
| [Co(thalvan)]                    | 3C           | 9                                    | 8                                       |
| [Ni(thalvan)](AcO <sup>-</sup> ) | 4C           | 8                                    | -ve                                     |
| [Cu(thalvan)](AcO <sup>-</sup> ) | 5C           | 15                                   | 12                                      |
| [Zn(thalvan)]                    | 6C           | 7                                    | 8                                       |
| DMF                              | DMF          | -ve                                  | -ve                                     |
| Streptomycin                     | Strepto.     | 19                                   | 18                                      |

-ve (no antibacterial activity observed)



**Figure 10: The zone of inhibition in Antibacterial activity**

Figure 11, graphically shows antibacterial activity statistics of ligands and their coordinated complexes as follows:

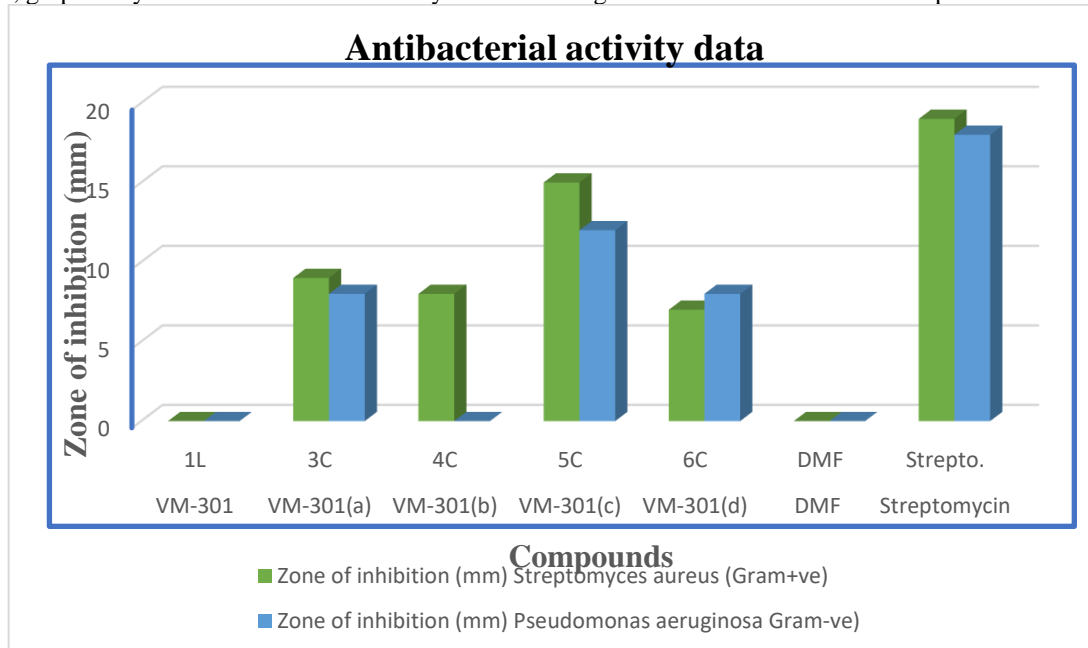


Figure 11: Graphical representation of antibacterial activity of thalvan ligand and its coordinated compounds.

## 5.2. Antioxidant activity

The study of azomethine and its coordinated Co(II), Ni(II), Cu(II), and Zn(II) complexes as antioxidants has led to many useful discoveries in the medical and pharmaceutical fields. These discoveries have mostly been made in vitro systems. Research has primarily focused on their potential applications and benefits, highlighting their effectiveness in various therapeutic contexts. These findings suggest a promising avenue for developing new antioxidant agents. The concentration 100 µg/mL is used carried out antioxidant activity and comparison against ascorbic acid (AA) and butylated hydroxyl toluene (BHT) as a drug standard. The investigation of antioxidant assay revealed that imines and their complexes showed potent to moderated scavenging activity but less as compared to standard.

### 5.2.1. DPPH radical scavenging activity

DPPH antioxidant method is rapid as well as simple i.e. not involved with many steps and not required more reagents to study as comparison to other radical scavenging method. DPPH is the most stable free

radical. It can easily take on an electron or hydrogen radical and change it into a stable molecule that is diamagnetic. DPPH exhibits a prominent peak at 517 nm. When an antioxidant agent is added to a fresh DPPH solution, its deep purple-blue colour vanishes. The decrease or reduction in absorbance is depending on more potent antioxidant present into the tested medium[36].

Generally, two step mechanisms occurs in the antioxidants scavenge free radicals. The first method depends removing hydrogen from the molecules, while the second method uses the proton to start transferring electrons immediately[37]. Initially Schiff base ligand showed moderate to least DPPH activity as compared to tested standard ascorbic acid (AA), however after complexation with metal ions the antioxidant activity was enhanced as compared previously.

The Cu(II) complex showed significantly higher DPPH activity than other complexes. The Zn(II) complex show less DPPH activity than free parent thalvan ligand and other complex. The statistics data of DPPH antioxidant assay is summarized in **Table 8**.

Table 8: DPPH antioxidant assay data of thalvan ligand and their coordinated compounds

| Compounds                        | % Inhibition |
|----------------------------------|--------------|
| Thalvan ligand                   | 42.9         |
| [Co(thalvan)]                    | 54.0         |
| [Ni(thalvan)](AcO <sup>-</sup> ) | 62.1         |
| [Cu(thalvan)](AcO <sup>-</sup> ) | 78.1         |
| [Zn(thalvan)]                    | 36.6         |
| AA                               | 86.4         |

When an antioxidant is present, the molecule quickly neutralizes the DPPH free radical, quenching the

measured medium's absorbance. The faster the drop, the stronger the antioxidant activity of the compound.

Among these Schiff base and their coordinated compounds, nickel and copper complexes showed good DPPH activity as compare to other parent ligand and complexes as but less than the standard ascorbic acid. The Zn(II) complex show less or equal antioxidant

activity to their free parent ligands. Figure 12, graphically shows DPPH antioxidant assay data of azomethine ligands and their coordinated molecules as follows:

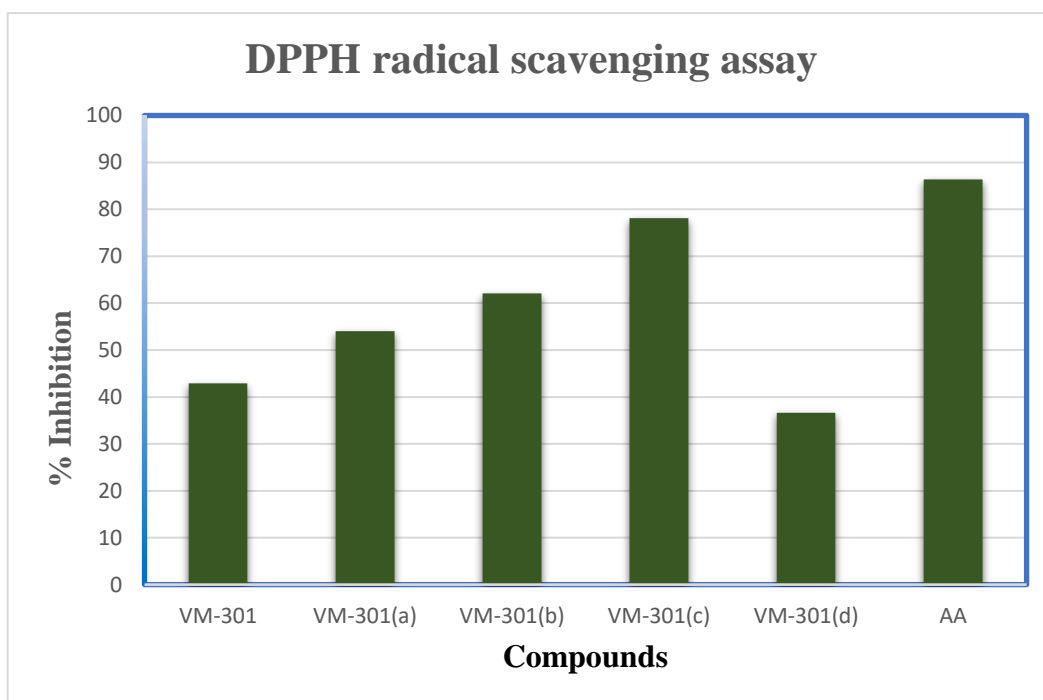


Figure 12: Graphical representation of antioxidant activity using DPPH, of thalvan ligand and its coordinated compounds.

**5.2.2. Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) antiradical activity**

Because of its poisonous and destructive effects, hydrogen peroxide targets numerous cellular energy production mechanisms[38]. The hydrogen peroxide easily produces the oxidizing enzymes like superoxide dismutase in biotic system. It shows cross cell layer and slow oxidizes which is used as activated phagocytes in respiratory burst. The hydrogen peroxide scavenging activity resulting data showed that Schiff base and their coordinated metal compounds exhibited a significant

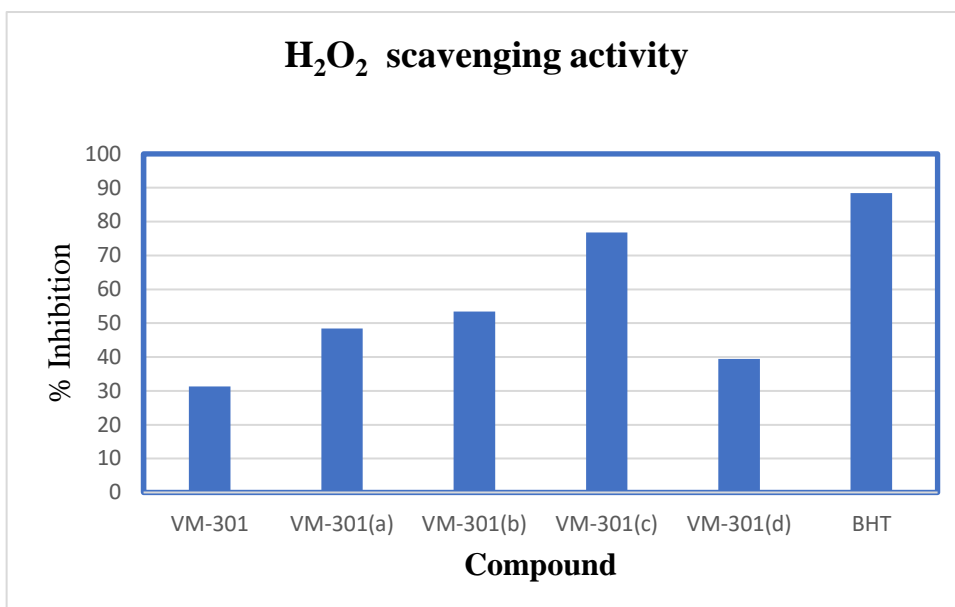
antioxidant assay. The results data of activity is summarized in Table 9. The antiradical assay of azomethine ligand enhanced on complexation with Co(II), Ni(II) and Cu(II) ions, While Zn(II) complex show near similar or equal to parent ligands. The Cu(II) complexes, VM-301(c) exhibited higher hydrogen peroxide activity as compared with other complexes but less than the standard BHT. The Schiff base compounds containing -OCH<sub>3</sub> groups in their structure exhibited an effective and more hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) scavenging activity.

Table 9: Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) scavenging assay data of thalvan ligand and their coordinated compounds.

| Compounds                        | % Inhibition |
|----------------------------------|--------------|
| Thalvan ligand                   | 31.3         |
| [Co(thalvan)]                    | 48.4         |
| [Ni(thalvan)](AcO <sup>-</sup> ) | 53.4         |
| [Cu(thalvan)](AcO <sup>-</sup> ) | 76.8         |
| [Zn(thalvan)]                    | 39.4         |
| BHT                              | 88.4         |

After the coordination with metal ions, Schiff base parent free ligands showed an active hydrogen peroxide antioxidant assay. The Cu(II) and Ni(II) complexes showed significant hydrogen peroxide scavenging assay. The free parent thalvan ligand show mild

scavenging activity. In the Zn(II) complex is least scavenging activity among all the complexes. Figure 13, graphically shows Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) antiradical action data of thalvan ligand and their coordinated molecules as follows:



**Figure 13:** Graphical representation of antioxidant activity using Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), of thalvan ligand and its coordinated compounds.

### Conclusion

This study validates the assemblies of the azomethine ligand and coordinated compounds by preparing cobalt, nickel, copper, and zinc coordinated compounds from a novel azomethine ligand and characterizing them using chemical composition, spectroscopy, vibrating sample magnetometer, and molar conductivity data. The bactericidal activity of the molecules was performed against *Streptomyces aureus* as monoderm and *Pseudomonas aeruginosa* as diderm bacteria strains in comparison to conventional pharmaceutical drugs streptomycin. The data showed that the bactericidal activity was enhanced when the ligand was complexed. The copper-coordinated complexes show higher bactericidal properties with both gram-positive and gram-negative bacteria. Using both DPPH and H<sub>2</sub>O<sub>2</sub> to test antioxidant activity shows that the copper-coordinated complex makes it work better. The ultrasonic methodology enhances the product preparation with excellent yield. The study results indicate that the ultrasonication method significantly improves yield and reduces reaction times compared to traditional synthesis techniques.

### Acknowledgements

Authors gratefully thank SAIF, IIT-Madras, STIC INDIA, Cochin, SAIF-Chandigarh, and CSIR-IICT Hyderabad for the VSM, ICPMS, NMR, and mass spectra, respectively. We are also grateful to the Head, PG Teaching Department of Chemistry, RTM Nagpur University, for the instrumental analysis and other laboratory help.

**Conflict of interest:** The author declares no conflict of interest.

### References

C. Boulechar *et al.*, "Schiff bases and their metal Complexes: A review on the history, synthesis, and applications," *Inorg Chem Commun*, vol. 150,

no. January, 2023, doi: 10.1016/j.inoche.2023.110451.

- [2] M. K. P. Irfankhan R. Pathan\*, "A comprehensive review on the synthesis and applications of Schiff base ligand and metal complexes: A comparative study of conventional heating, microwave heating, and sonochemical methods," *Inorg Chem Commun*, vol. 158, 2023.
- [3] J. C. Pessoa and I. Correia, "Salan vs. salen metal complexes in catalysis and medicinal applications: Virtues and pitfalls," *Coord Chem Rev*, vol. 388, pp. 227–247, 2019, doi: 10.1016/j.ccr.2019.02.035.
- [4] E. M. Abdalla, L. H. Abdel Rahman, A. A. Abdelhamid, M. R. Shehata, A. A. Allothman, and A. Nafady, "Synthesis, Characterization, Theoretical Studies, and Antimicrobial/Antitumor Potencies of Salen and Salen/Imidazole Complexes of Co (II), Ni (II), Cu (II), Cd (II), Al (III) and La (III)," *Appl Organomet Chem*, vol. 34, no. 11, pp. 1–22, 2020, doi: 10.1002/aoc.5912.
- [5] J. Fonseca, J. Martinez, L. Cunha-Silva, A. L. Magalhães, M. T. Duarte, and C. Freire, "Insights into electronic and structural properties of novel Pd(II) salen-type complexes," *Inorganica Chim Acta*, vol. 363, no. 14, pp. 4096–4107, 2010, doi: 10.1016/j.ica.2010.08.023.
- [6] V. Lorenz, P. Liebing, L. Hilfert, S. Busse, and F. T. Edelmann, "An unsymmetrical dinuclear scandium complex comprising salophen ligands [H<sub>2</sub> salophen = N, N'-bis(salicylidene)-1,2-phenylenediamine]," *Acta Crystallogr E Crystallogr Commun*, vol. 75, pp. 175–178, 2019, doi: 10.1107/S2056989019000094.
- [7] A. N. M. A. Alaghaz, M. E. Zayed, and S. A. Alharbi, "Synthesis, spectral characterization, molecular modeling and antimicrobial studies of tridentate azo-dye Schiff base metal complexes," *J Mol Struct*, vol. 1084, pp. 36–45, Mar. 2015, doi: 10.1016/J.MOLSTRUC.2014.12.013.

- [8] N. K. Chaudhary, B. Guragain, S. K. Chaudhary, and P. Mishra, "Schiff base metal complex as a potential therapeutic drug in medical science: A critical review," *Bibechana*, vol. 18, no. 1, pp. 214–230, 2021, doi: 10.3126/bibechana.v18i1.29841.
- [9] S. S. Pasha, H. R. Yadav, A. R. Choudhury, and I. R. Laskar, "Synthesis of an aggregation-induced emission (AIE) active salicylaldehyde based Schiff base: Study of mechanoluminescence and sensitive Zn(II) sensing," *J Mater Chem C Mater*, vol. 5, no. 37, pp. 9651–9658, 2017, doi: 10.1039/c7tc03046k.
- [10] W. H. Mahmoud, R. G. Deghadi, and G. G. Mohamed, "Novel Schiff base ligand and its metal complexes with some transition elements. Synthesis, spectroscopic, thermal analysis, antimicrobial and in vitro anticancer activity," *Appl Organomet Chem*, vol. 30, no. 4, pp. 221–230, 2016, doi: 10.1002/aoc.3420.
- [11] H. P. Gogoi, N. Goswami, A. Singh, and P. Barman, "Microwave-assisted synthesis of Schiff base metal complexes: Biological, photocatalytic activity and fabrication of their metal oxide nanoparticles," *J Mol Struct*, vol. 1303, p. 137583, May 2024, doi: 10.1016/J.MOLSTRUC.2024.137583.
- [12] A. Ahmad *et al.*, "Ultrasonic assisted synthesis, characterization and bioactivity assessment of novel piperonal based schiff base and its metal complexes," *Iranian Journal of Chemistry and Chemical Engineering*, vol. 39, no. 2, pp. 105–111, 2020, doi: 10.30492/IJCCE.2020.33369.
- [13] S. Nagar, S. Raizada, and N. Tripathi, "A review on various green methods for synthesis of Schiff base ligands and their metal complexes," *Results Chem*, vol. 6, no. September, p. 101153, 2023, doi: 10.1016/j.rechem.2023.101153.
- [14] A. Mermer *et al.*, "Synthesis of novel Schiff bases using green chemistry techniques; antimicrobial, antioxidant, antiurease activity screening and molecular docking studies," *Molecular structure*, 2019.
- [15] N. Turan, M. BiNgöl, A. Savci, E. F. Koçpinar, and N. Çolak, "Synthesis, structural studies and antioxidant activities of M(II) complexes with NOS donor schiff base ligand," *Sigma Journal of Engineering and Natural Sciences*, vol. 39, no. 3, pp. 279–289, 2021, doi: 10.14744/sigma.2021.00017.
- [16] T. E. Olalekan, A. S. Ogunlaja, B. VanBrecht, and G. M. Watkins, "Spectroscopic, structural and theoretical studies of copper(II) complexes of tridentate NOS Schiff bases," *J Mol Struct*, vol. 1122, pp. 72–79, Oct. 2016, doi: 10.1016/J.MOLSTRUC.2016.05.098.
- [17] C. Enol, Z. Hayvali, H. Dal, and T. Hökelek, "Syntheses, characterizations and structures of NO donor Schiff base ligands and nickel(II) and copper(II) complexes," *J Mol Struct*, vol. 997, no. 1–3, pp. 53–59, 2011, doi: 10.1016/j.molstruc.2011.04.037.
- [18] A. Z. El-Sonbati, W. H. Mahmoud, G. G. Mohamed, M. A. Diab, S. M. Morgan, and S. Y. Abbas, "Synthesis, characterization of Schiff base metal complexes and their biological investigation," *Appl Organomet Chem*, vol. 33, no. 9, pp. 1–16, 2019, doi: 10.1002/aoc.5048.
- [19] D. Aggoun *et al.*, "New nickel (II) and copper (II) bidentate Schiff base complexes, derived from dihalogenated salicylaldehyde and alkylamine: Synthesis, spectroscopic, thermogravimetry, crystallographic determination and electrochemical studies," *Polyhedron*, vol. 187, Sep. 2020, doi: 10.1016/j.poly.2020.114640.
- [20] Ah. A. H. Abdellatif *et al.*, "Recent Advances in the Pharmaceutical and Biomedical Applications of Cyclodextrin-Capped Gold Nanoparticles," *Int J Nanomedicine*, vol. 18, pp. 3247–3281, 2023, doi: 10.2147/IJN.S405964.
- [21] A. K. and S. J. \*† Shubhangi Borse,† MayurTemgire, "Photochemically assisted one-pot synthesis of PMMA embedded silver nanoparticles: Antibacterial efficacy and water treatment," *RSC Adv*, vol. 3, 2016, doi: 10.1039/b000000x.
- [22] F. Arjmand, B. Mohani, and S. Ahmad, "Synthesis, antibacterial, antifungal activity and interaction of CT-DNA with a new benzimidazole derived Cu(II) complex," *Eur J Med Chem*, vol. 40, no. 11, pp. 1103–1110, 2005, doi: 10.1016/j.ejmech.2005.05.005.
- [23] A. M. Elseman, A. E. Shalan, M. M. Rashad, A. M. Hassan, N. M. Ibrahim, and A. M. Nassar, "Easily attainable new approach to mass yield ferrocenyl Schiff base and different metal complexes of ferrocenyl Schiff base through convenient ultrasonication-solvothermal method," *J Phys Org Chem*, vol. 30, no. 6, pp. 1–10, 2017, doi: 10.1002/poc.3639.
- [24] S. K. Tadavi, A. A. Yadav, and R. S. Bendre, "Synthesis and characterization of a novel schiff base of 1,2-diaminopropane with substituted salicylaldehyde and its transition metal complexes: Single crystal structures and biological activities," *J Mol Struct*, vol. 1152, pp. 223–231, Jan. 2018, doi: 10.1016/j.molstruc.2017.09.112.
- [25] S. Poola *et al.*, "Nano CuO–Ag-catalyzed synthesis of some novel pyrano[2,3-d] pyrimidine derivatives and evaluation of their bioactivity," *Journal of the Chinese Chemical Society*, vol. 67, no. 5, pp. 805–820, 2020, doi: 10.1002/jccs.201900256.
- [26] M. N. Alam, N. J. Bristi, and M. Rafiqzaman, "Review on in vivo and in vitro methods evaluation of antioxidant activity," *Saudi Pharmaceutical Journal*, vol. 21, no. 2, pp. 143–152, 2013, doi: 10.1016/j.jsps.2012.05.002.
- [27] A. Bag, S. Kumar Bhattacharyya, N. Kumar Pal, and R. R. Chattopadhyay, "Anti-inflammatory, anti-lipid peroxidative, antioxidant and membrane stabilizing activities of hydroalcoholic extract of Terminalia chebula fruits," *Pharm Biol*, vol. 51,



- no. 12, pp. 1515–1520, 2013, doi: 10.3109/13880209.2013.799709.
- [28] S. S. Konstantinović and V. S. Cakić, “Pharmacological characteristics of some 3-salicylidenehydrazono-2-indolinone coordination compounds,” *Medicinal Chemistry Research*, vol. 19, no. 8, pp. 771–781, 2010, doi: 10.1007/s00044-009-9229-1.
- [29] B. S. Creaven *et al.*, “Quinolin-2(1H)-one-triazole derived Schiff bases and their Cu(II) and Zn(II) complexes: Possible new therapeutic agents,” *Polyhedron*, vol. 29, no. 2, pp. 813–822, 2010, doi: 10.1016/j.poly.2009.11.002.
- [30] Z. H. Chohan, C. T. Supuran, and A. Scozzafava, “Metalloantibiotics: Synthesis and antibacterial activity of Cobalt(II), Copper(II), Nickel(II) and Zinc(II) complexes of kefzol,” *J Enzyme Inhib Med Chem*, vol. 19, no. 1, pp. 79–84, 2004, doi: 10.1080/14756360310001624939.
- [31] B. Rodríguez, M. Pastó, C. Jimeno, and M. A. Pericàs, “Parallel synthesis of modular chiral Schiff base ligands and evaluation in the titanium(IV) catalyzed asymmetric trimethylsilylcyanation of aldehydes,” *Tetrahedron Asymmetry*, vol. 17, no. 1, pp. 151–160, 2006, doi: 10.1016/j.tetasy.2005.11.022.
- [32] R. Bhaskar, N. Salunkhe, A. Yaul, and A. Aswar, “Bivalent transition metal complexes of ONO donor hydrazone ligand: Synthesis, structural characterization and antimicrobial activity,” *Spectrochim Acta A Mol Biomol Spectrosc*, vol. 151, pp. 621–627, 2015, doi: 10.1016/j.saa.2015.06.121.
- [33] K. Mohanan and B. Murukan, “Complexes of manganese(II), iron(II), cobalt(II), nickel(II), copper(II), and zinc(II) with a bishydrazone,” *Synthesis and Reactivity in Inorganic, Metal-Organic and Nano-Metal Chemistry*, vol. 35, no. 10, pp. 837–844, 2005, doi: 10.1080/15533170500357988.
- [34] M. S. Al-Fakeh, M. A. Alsikhan, and J. S. Alnawmasi, “Physico-Chemical Study of Mn(II), Co(II), Cu(II), Cr(III), and Pd(II) Complexes with Schiff-Base and Aminopyrimidyl Derivatives and Anti-Cancer, Antioxidant, Antimicrobial Applications,” *Molecules*, vol. 28, no. 6, 2023, doi: 10.3390/molecules28062555.
- [35] M. Gaber, K. El-Baradie, N. El-Wakiel, and S. Hafez, “Synthesis and characterization studies of 3-formyl chromone Schiff base complexes and their application as antitumor, antioxidant and antimicrobial,” *Appl Organomet Chem*, vol. 34, no. 2, pp. 1–15, 2020, doi: 10.1002/aoc.5348.
- [36] A. C. Ekennia, A. A. Osowole, L. O. Olasunkanmi, D. C. Onwudiwe, and E. E. Ebenso, “Coordination behaviours of new (bidentate N,O-chelating) Schiff bases towards copper(II) and nickel(II) metal ions: synthesis, characterization, antimicrobial, antioxidant, and DFT studies,” *Research on Chemical Intermediates*, vol. 43, no. 7, pp. 3787–3811, 2017, doi: 10.1007/s11164-016-2841-z.
- [37] D. Mikulski and M. Molski, “Quantitative structure-antioxidant activity relationship of trans-resveratrol oligomers, trans-4,4'-dihydroxystilbene dimer, trans-resveratrol-3-O-glucuronide, glucosides: Trans-piceid, cis-piceid, trans-astringin and trans-resveratrol-4'-O-β-D-glucopyran,” *Eur J Med Chem*, vol. 45, no. 6, pp. 2366–2380, 2010, doi: 10.1016/j.ejmech.2010.02.016.
- [38] Y. Harinath, D. Harikishore Kumar Reddy, B. Naresh Kumar, C. Apparao, and K. Seshaiiah, “Synthesis, spectral characterization and antioxidant activity studies of a bidentate Schiff base, 5-methyl thiophene-2-carboxaldehyde-carbohydrazone and its Cd(II), Cu(II), Ni(II) and Zn(II) complexes,” *Spectrochim Acta A Mol Biomol Spectrosc*, vol. 101, pp. 264–272, 2013, doi: 10.1016/j.saa.2012.09.085