ORIENTAL JOURNAL OF CHEMISTRY
An International Open Access, Peer Reviewed Research Journal
www.orientjchem.org
ISSN: 0970-020 X
CODEN: OJCHEG
2025, Vol. 41, No.(3):
Pg. 921-926

Antimicrobial and Anti-arthritic Studies of Metal (II) Complexes of Schiff base Derived from 2-Hydroxy-1-Naphthaldehyde

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http://dx.doi.org/10.13005/ojc/410324

(Received: December 16, 2024; Accepted: May 14, 2025)

ABSTRACT

Copper(II), Zinc(II), and Cobalt(II) complexes of Schiff base derivatives of 2-hydroxy-1-naphthaldehyde with 4-bromo aniline were prepared for the current study. These complexes were then characterized using several spectrum analyses, including UV-Vis spectra, FTIR spectra, ^{1}HNMR, ^{13}CNMR and XRD. The disc diffusion method was used to assess the bacterial activity. The complexes showed more antibacterial activity than the ligand. Many useful anti-cancer metal-based drugs have been introduced. However, less attention has been paid to the improvement of anti-arthritic drugs based on metal complexes. So, anti-arthritic properties were computed. The synthesized compounds were evaluated for their anti-arthritic by using egg albumin denaturation method. It was found that copper complex had the lowest IC_{50} value (6.53 µg/mL) and hence was the most active one. These findings support the use of schiff base complex in the management of long-term inflammatory conditions and suggest that it may be a candidate for the discovery of novel anti-arthritic chemicals.

Keywords: Schiff base, 2-Hydroxy-1-naphthaldehyde, Transition metal(II) complexes, Antimicrobial, Anti-arthritic activity.

INTRODUCTION

Schiff bases are created when amines combine with aldehydes or ketones to produce azomethine or imine groups[1]. Because they are biologically active substances, these Schiff bases are widely used as pharmaceuticals[2,3]. The carbon-nitrogen double bond (C=N), which can bind with metal, makes schiff bases significant[4]. Numerous biological actions, including antifungal, analgesic, anti-inflammatory, antibacterial, antioxidant, anticancer, cardiovascular, and antitubercular properties, have been documented for these significant compounds[5–8]. Schiff base ligands can pair with a wide range of metals in different oxidation states[9]. 2-hydroxy-1-naphthaldehyde is used as an important precursor for the synthesis of various biologically active compounds. Its derivatives have been found to antimicrobial, antioxidant, anticancer and antiulcer activities[10]. The effectiveness of such compounds increases when coordinated to metal ions[11]. Here some metal complexes of schiff base derivatives of 2-hydroxy-1-naphthaldehyde with 4-bromo aniline were prepared. After synthesizing the Schiff base 1-(((4-bromophenyl)

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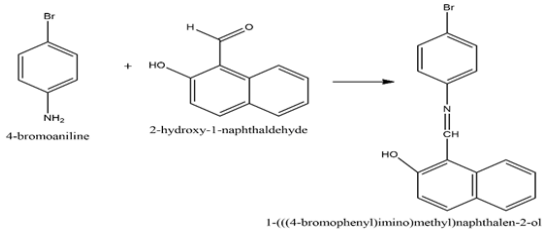
imino)methyl)naphthalen-3-ol), ^{13}C NMR and $^{1}HNMR$ spectroscopy, UV, XRD were used to determine the molecular structure. The prepared Schiff base's and its metal complexes' antibacterial and anti-arthritic properties were examined.

MATERIALS AND METHODS

Sigma Aldrich provided the 2-hydroxy-1-naphthaldehyde and 4-bromo aniline. By condensing 2-hydroxy-1-naphthaldehyde (0.01 mol) and 4-bromo aniline (0.01 mol) for four to five hours at 40 to 50 degrees Celsius, the Schiff base ligand is created. The yellow solid product that is left over after the reaction is finished. Scheme I illustrates the synthesis. The Schiff base ligand's ^{13}C and ^{1}H spectra are displayed in Fig. 1(a & b). Schiff base and its metal complexes analysed by XRD, UV-Vis spectra and CHN analysis.



Scheme 1. Synthesis of SB

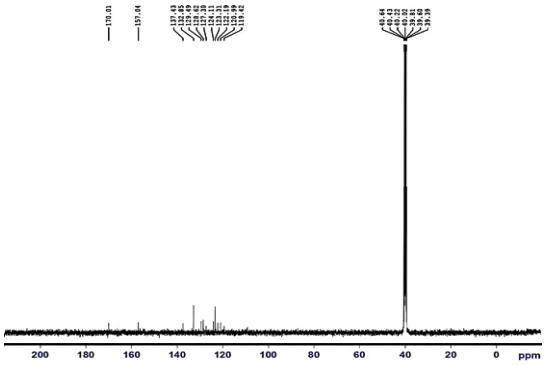


Fig. 1(a). ^{13}C spectrum of SB

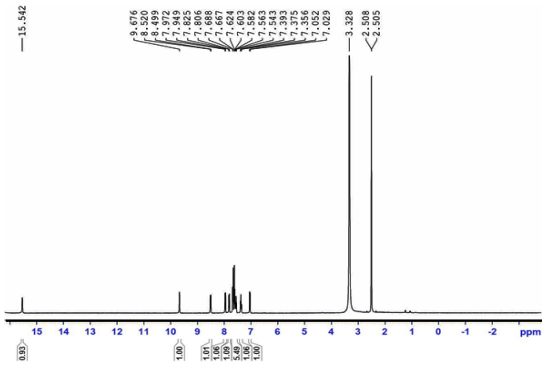


Fig. 1(b). ^{1}H spectrum of SB

Synthesis of Schiff base metal complexes

After dissolving the Schiff base and metal chloride salt in an ethanolic solution at a 1:2 (M:L) molar ratio, refluxed for four to five hrs. at 50 to 60°C. The resulting complex is properly filtered and then washed with ethanol before being thoroughly dried at 20 to 25°C. On anhydrous $CaC1_2$, stable and coloured metal complexes are maintained in desiccators.

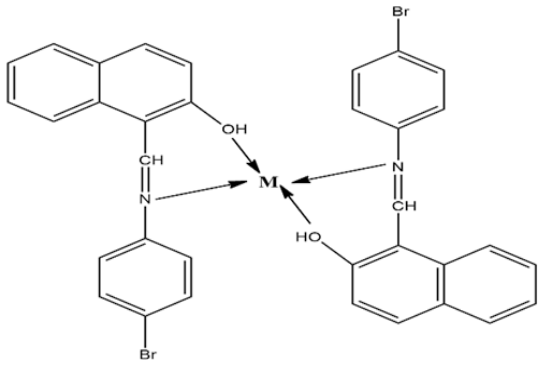


Fig. 2. Structure of complex (M= Cu^{2+}, Co^{2+}, Zn^{2+})

In-vitro anti-arthritic activity

The egg albumin denaturation method was used to investigate the *in vitro* anti-arthritic activity[12,13]. 2.8 millilitres of PBS, 0.2 millilitres of egg albumin, and 2 millilitres of ligand/metal complex in various concentrations (10, 20, 30, 40, and 50 µg/mL). Use the same mixture to prepare a standard solution. The control was given a comparable volume of double-distilled water, which indicates 100% denaturation. After 15 min at 37±2°C, the aforementioned mixes were heated for 5 min at 70°C. Six times of the test process were conducted. Following cooling, the abs. was observed by UV Spec. at 660 nm. The percentage inhibition of denaturation, a measure of anti-arthritic activity, can be calculated by:

$$\%Inhibition = 100 \times (V_t/V_c\text{-}1)$$

Assay of Antibacterial Activity

After the original Bauer *et al.,* (1966) method was modified, an antibacterial activity test was conducted[14]. Muller Hinton agar was made, autoclaved for 20 min at 15 pounds of pressure, and then cooled to 45 degrees Celsius. After cooling, the media was transferred onto sterile Petri plates and left to solidify. Using a sterile swab, the appropriate microbial suspension was applied to the media-containing plates. On each Petri plate, the different solvent extract-prepared discs were arranged separately, along with the control and standard (Ciprofloxacin (5 mcg) for Bacteria discs).

For twenty-four hours, the plates were incubated at 37°C. The zone inhibition calculated and reported in millimetres following the incubation period.

RESULTS AND DISCUSSION

Analytical Data

The analytical data obtained for the schiff base and complexes synchronize very well with the intended molecular formula and also designate the formation of 1:2 (M:L) transition metal complexes. The molar conductivity of the complexes is conceded out in DMSO at 20-25°C and is referred in Table 1. The obtained conductance values revealed the non-electrolytic nature and neutral character of metal complexes.

Table 1: Physical Characteristics and analytical data of Schiff base and its complexes

Sr. No	Schiff base & Complexes	Molecular Formula	Elemental analysis % Found			Metal%	Molar conductance
			C	H	N		
1	Schiff base	$C_{17}H_{12}BrNO$	62.56	3.71	4.33	-	-
2	Co complex	$[Co(C_{17}H_{12}BrNO)_2]$	57.41	3.40	3.94	8.29	17.42
3	Zn complex	$[Zn(C_{17}H_{12}BrNO)_2]$	56.89	3.37	3.90	9.11	11.68
4	Cu complex	$[Cu(C_{17}H_{12}BrNO)_2]$	57.01	3.41	3.91	8.82	15.60

^{1}H-NMR spectrum analysis

The synthesized compound's ^{1}H NMR spectra were captured in DMSO-d6 (500MHz) as the solvent, as shown in Fig. 1(b). Aromatic protons are responsible for the area at δ 7.54-7.65 ppm (s, 6H, aromatic rings)[15,16]. δ at 9.67 ppm (s, H, CH=N). The synthesized compound's ^{1}H NMR spectra reveal a signal at δ 9.67 ppm caused by phenolic OH. Naphthalene ring chemical shifts in the ^{13}CNMR spectrum from 119.42 to 137.43 (C1–C10) are identified as being 157.0 because of the carbon assigned at deshielding CH=N. NMR spectral study offered a comprehensive account which found to be acceptable for assignment of protons (1H). The observed ^{1}H NMR spectra of Schiff base ligand are given in Fig.1(b). The coordination of the azomethine nitrogen is inferred by the upfield shifting of -CH=N- proton signal from 9.676 in the ligand to 9.688 ppm in the Zn complex.

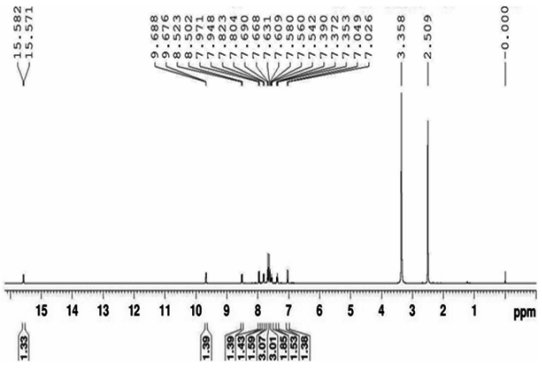


Fig. 3. ^{1}H spectrum of Zn complex

UV-Visible spectra

Figure 4 displays the results of UV-Visible experiments conducted in DMSO. According to the absorption wavelength values, the SB is identified at 220 (n→π), 224 (n→π), and 348 nm (n→π*) by bands. It was discovered that the chromphoric groups (imine and aromatic ring) in the ligand are responsible for the n→π* and n→π* transitions. It was discovered that the values were near the four coordinate system when the observed values were compared to values published in the literature.

FT-IR spectra

The significant FT-IR vibrational spectral frequencies of ligand as well as complexes are measured in 400-4000 cm^{-1} region. The observed FT-IR spectra are illustrated in Fig. 5. The CH stretching vibration spectra of ligand and metal complexes are assigned at 3060-3232 cm^{-1}. The coordination of metal through the N and O atoms of anthracene ring cause significant changes in the bands arrived for ligand after the complexation, which was evident from IR bands of both ligand and metal complexes. The CN stretching vibrations bands are originated at 1689 cm^{-1} (ligand), 1664 cm^{-1} (Zn(II)), 1668 cm^{-1} (Cu(II)) and 1630 cm^{-1} (Co(II)). Furthermore, bending vibration frequencies of NC are arrived at 966 (ligand), 956 (Z(II)), 959 (Cu(II)) and 951 (Co(II)) cm^{-1}. Besides, the CO stretching vibrations are assigned at 1260 (ligand), 1245 (Zn(II)), 1246 (Cu(II)) and 1241 (Co(II)) cm-1. It is noted that, the band is moved towards the lesser frequency after complexation.

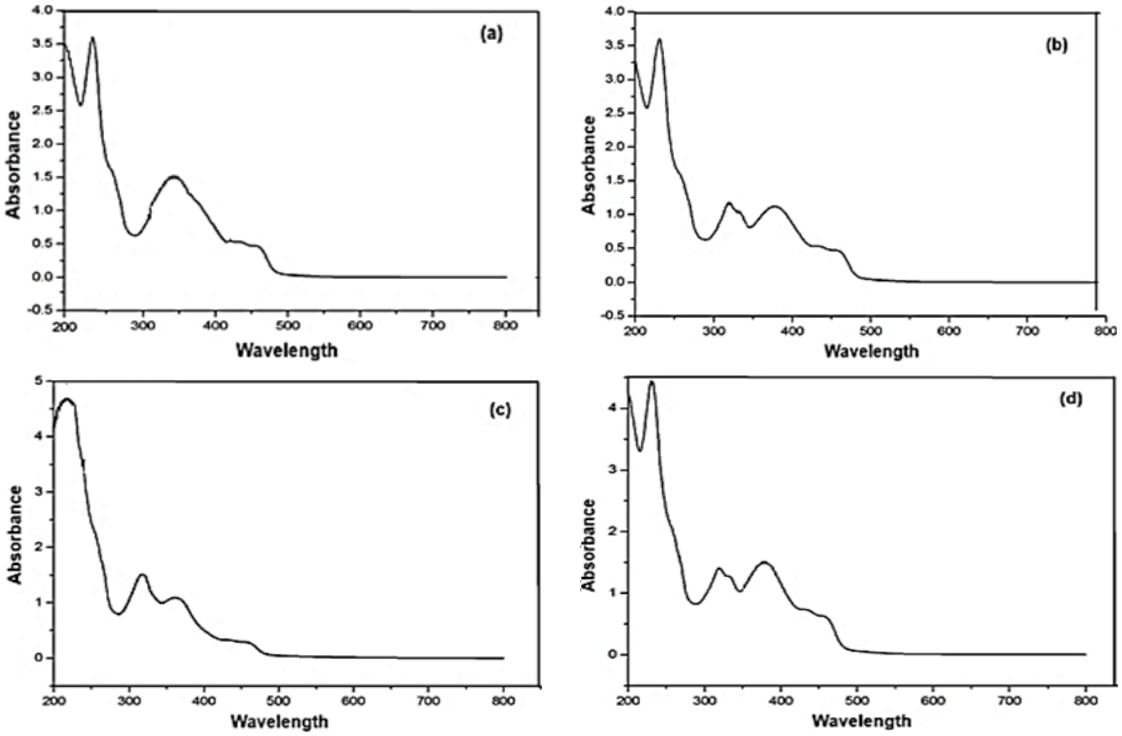


Fig. 4. UV-Visible spectra of (a) SB (b) Cu (c) Zn (d) Co complex

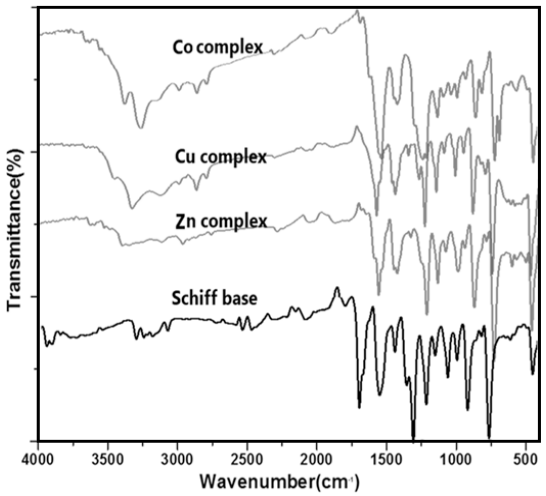


Fig. 5. FT-IR spectral of Schiff base ligan and its metal complex

XRD analysis

XRD spectra for Schiff base, cobalt complex, zinc complex and copper complexes were recorded and shown in Fig. 6. XRD study of Copper complex displays sharp, crystalline peaks indicating their crystalline nature, peak expansion in all other complexes due to their amorphous character. The average crystallite size of Schiff base and metal complex was calculated using Scherer formula given in Eq. (1):

$$L = \frac{0.89\lambda}{\beta \cos\theta} \quad (1)$$

Where *L* is the crystallite size, λ, the X-ray wavelength, θ, the Bragg diffraction angle and β, the full width at half maximum (FW-HM). The Schiff base, cobalt complex, zinc complex and copper complexes comprise an average crystalline size of 51.8nm,15.2nm, 35.5nm and 50.2nm, respectively.

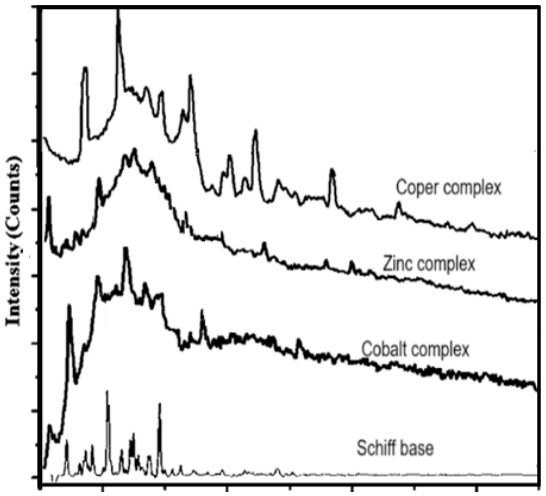


Fig. 6. XRD studies of Schiff base and its metal complexes

Magnetic properties

The magnetic moment values obtained for

the binuclear complexes are slightly different from expected due to the interaction between the ligand metal ions, indicating the possibility of a spin-coupled system. The obtained magnetic moment value of Co(II), Cu(II) are 3.78B.M., 1.84B.M., respectively, and referred to as Co(II), Cu(II) metal centre as paramagnetic and was distorted from tetrahedral symmetry to the square planar. Meanwhile, the metal centre of Zn(II)showed the magnetic nature of diamagnetic. Higher magnetic moments (3.78 BM) are attributed to distorted tetrahedral configurations and lower magnetic moments (1.84 BM) are due to square-planar configurations[17].

Antibacterial activity

Antibacterial activity was measured by using the disc diffusion method, shown in Table 2, it was found that the lipophilic character of the complexes revealed more antibacterial activity than the ligand.

Table 2: Antibacterial activity of SB and complexes

Sr. No	Bacteria	Zone inhibition in mm					
		C	Std	SB	Cu cmplx	Zn cmplx	Co cmplx
1	*Bacillus subtilis*	-	22	14	16	14	14
2	*Escherichia coli*	-	21	14	18	16	15
3	*Staphylococcus aureus*	-	12	8	10	9	9

Anti-arthritic screening

Based on their inhibition of protein denaturation, the compounds had moderate antiarthritic efficacy, according to the results shown in Table 3. For example, the copper complex's IC_{50} value is 6.53, whereas the normal diclofenac sodium salt's IC_{50} value is 0.563.

Table 3: Anti-arthritic activity of metal complex compared with standard

Concentration(µg/mL)	% of Inhibition Diclofenac Na (Standard)	% of Inhibition of copper complex	% of Inhibition of cobalt complex	% of Inhibition of zinc complex
20	56.28	55.5	60.28	40.2
40	60.14	58.2	65.4	62.82
60	67.49	65.41	70,18	69.21
80	72.78	70.12	74.9	70.34
100	78.69	76.9	81.54	80.24
IC_{50} value	0.563	6.53	156.93	26.75

Inflammation is a normal protective response to tissue injury caused by physical trauma, noxious chemical or microbial agents. It is the body response to inactivate or destroy the invading organisms, to remove the irritants and set the stage for tissue repair. It is triggered by the release of chemical mediators from injured tissue and migrating cells[18]. Prolonged inflammation leads to the auto-immune diseases like rheumatoid arthritis (RA), atherosclerosis[19,20]. The inflammation of RA can also occur in tissues around the joints, ligaments and muscles[21]. Inflammation is usually associated with the denaturation of proteins. Results from the present study revealed that metal complexes significantly inhibited protein/albumin denaturation. Copper metal complex showed better efficacy (IC_{50} value 6.53) than zinc metal complex (IC_{50} value 26.75) and cobalt metal complex (IC_{50} value 156.93). Worldwide, rheumatoid arthritis is a major cause of morbidity and mortality. In recent years, the domain of inorganic medicinal chemistry has shown more interest in metal-based drugs owing to their beneficial pharmacological activities[22]. To find new treatments for diseases, it is suggested that the mechanism of action and potential toxicity of metal complexes must be assessed.

CONCLUSION

Schiff base successfully synthesised by condensation of 2-hydroxy-1-naphthaldehyde with 4-bromo aniline. Using the appropriate metal (II) chlorides, this ligand was complexed with copper, zinc, and cobalt. Numerous spectrum analyses have suggested that azomethine nitrogen (-C=N-) and phenolic oxygen (-OH) coordinate with metals. The complexes' antibacterial activity has demonstrated notable activity. The commonly used drug for

management of inflammatory conditions are non-steroidal anti-inflammatory drugs (NSAIDs), which have several adverse effects especially gastric irritation leading to formation of gastric ulcers. For these reason, there is a need for ant-inflammatory drugs having less severe side effects to use for chronic inflammatory disease as well. Protein denaturation was studied to further establish the mechanism of anti-inflammatory action. Among the all complexes studied, copper compound showed the most anti-arthritic effect. The synthesized complexes have demonstrated effective biological activity, according to the results reported here.

ACKNOWLEDGEMENT

The authors thankful to SIF, VIT, Vellore for spectral studies.

Conflict of interest

The authors declare that there is no conflict of interest.

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