



## African Journal of Biological Sciences



# Studies On Antimicrobial, Antifungal And Anti-Inflammatory Activities Of New Synthesized Schiff Base And Its Metal Complexes

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#### Article History

Volume 6, Issue Si4, 2024

Received: 15 July 2024

Accepted: 26 July 2024

Published: 2 Aug 2024

Doi:

10.48047/AFJBS.6.Si4.2024.5217-5230

#### Abstract

Throughout the annals of human history, infectious diseases have occupied a central position, shaping societies, driving progress in medicine, and profoundly affecting the health of people globally. So, in the pursuit of noteworthy biological compounds, synthesis of a novel Schiff Base involved the condensation of 4-hydroxy benzaldehyde with octadecylamine, which subsequently interacted with the salts of Cu (II) and Ba (II) metals to generate their respective complexes. Different analytical methods, such as NMR (<sup>1</sup>H and <sup>13</sup>C), IR, molar conductance, elemental analysis, and mass spectrometry, which indicates the complexes' tetrahedral stereochemistry via the N- and Cl-atoms of the ligands, were used to thoroughly characterize the compounds. Additionally, the bovine serum albumin (BSA) and serial dilution techniques were used to examine their therapeutic efficacy against bacterial, fungal, and inflammatory diseases. The protocols implemented demonstrated that the ligand's inhibitory characteristic was amplified upon complexation with a metal. The Ba-Schiff Base complex exhibits the greatest efficacy against bacterial and fungal pathogens, as evidenced by its antibacterial and antifungal activities. Its Minimum Inhibitory Concentration (MIC) values range from 0.0065 to 0.0141  $\mu\text{mol/mL}$ , and it is found to be highly active against *C. albicans*, with a value of 0.0065  $\mu\text{mol/ML}$ . BSA revealed that the Ba-Schiff Base complex demonstrates the lowest  $\text{IC}_{50}$  value of  $07.25 \pm 0.18 \mu\text{M}$ , signifying its superior efficacy for inflammatory conditions. The antibacterial, antifungal and anti-inflammatory activities are well consistent with each other, stating the highest potency of Ba-Schiff Base complex for use as medicinal agent.

**Keywords:** Schiff base; Metal complex; Characterization; Antibacterial; Anti-inflammatory

#### Introduction

The 18<sup>th</sup> century saw the emergence of medicinal chemistry in a vibrant scientific setting. Several scientists have worked to create and synthesized bioactive substances and pharmacological agents that are important to biological processes in living things, including the human body. These

substances, referred to as "drugs," cause beneficial biochemical reactions in living things. Medicinal chemistry's main aim is to study how medications interact with cells, with a particular emphasis on biochemical processes. The pharmaceutical business uses a wide range of chemicals with positive therapeutic indexes and low cytotoxicity as medications. Pathogenic microorganisms pose significant threats to living beings, causing mortality and morbidity worldwide. Consequently, up to 1928, discovery of penicillin and the 1930 discovery of sulfa medicines, a variety of bioactive substances, including plant extracts, were used to treat a wide range of microbiological infections. Aspirin is a common anti-inflammatory drug used in modern medicine to help the body rid itself of toxic substances and injured tissues, which helps treat a variety of ailments. By changing cell walls, synthetic, natural, and semi-synthetic substances with distinct processes can change physiological and metabolic levels. On the other hand, overuse of these substances can have detrimental effects on physiological processes, including aging, cell damage, organ failure, and occasionally even death. As such, the synthesis of pharmacological compounds with decreased toxicity to biological systems is critically needed.

Schiff bases are made up of structurally similar azomethine or imine groups ( $-\text{HC}=\text{N}-$ ). Primary amines and carbonyl compounds undergo a condensation process to produce Schiff bases. Hugo Schiff was the first to report these compounds, hence the term "Schiff base" [1]. Even when these condensation processes are conducted at room temperature, they can provide large yields and necessitate short reaction durations [2]. Without taking Schiff bases into account, the study of biological processes and catalysis will remain inadequate [3]. Researchers are drawn to Schiff base ligands because of their great propensity for coordination with different metals and their therapeutic significance. Copper was primarily utilized in antiquity as an antibacterial agent to purify water, and Cu(II) complexes provide a wide range of therapeutic benefits with lower toxicity [4]. Treatment effectiveness is declining in part because of the concerning growth in the number of bacteria that are resistant to a wide range of antibiotics and cannot be treated [5]. In both homogeneous and heterogeneous processes, Schiff base complexes of metal ions can be employed as catalysts to increase yield and product selectivity [6]. Because it can give us some suggestions for creating better molecular catalysts in the future, mechanistic study on proton reduction catalysis is essential [7]. For the first time, the Schiff base Cu(II) complexes were used as catalysts with CO<sub>2</sub> and oxirane to produce appropriate cyclic carbonates [8]. One-dimensional nanorods, non-conjugated polymer nanoclusters, and covalent organic frameworks (COFs) are among the nanostructure materials that have been successfully created in situ using Schiff Base chemistry [9]. Schiff base metal complexes can be used as antioxidant, antimicrobial, anti-inflammatory, anticancer, anti-tuberculosis agent [10–20].

Inspired by the current scenario, in this study a Schiff base, 4-((octadecylimino)methyl)phenol their metal complexes were synthesized which characterized by elemental analysis, molar conductivity, NMR, IR, & mass spectrometry. The complexes' tetrahedral structure was shown by the characterization data. Additionally, serial dilution & bovine serum albumin investigations were executed to assess their efficacy in inhibiting the development of bacteria, fungi, and inflammation in the hopes of discovering a major therapeutic agent.

## Experimental

### Materials and Instrumentations

The AR grade chemicals and reagents, obtained from the Sigma Aldrich company, included 2-hydroxybenzaldehyde (>99%), octadecyl amine (>99%), glacial acetic acid (>98%), copper chloride

(>99%), barium chloride (>99%), and ethanol (>99%). Next, octadecyl amine and 4-hydroxybenzaldehyde underwent a condensation process to synthesize a Schiff base.

### Instrumentation

The Avance III 400-MHz NMR apparatus (Bruker, MA, USA) was used to perform  $^{13}\text{C}$  and  $^1\text{H}$  NMR studies on produced Schiff Base and its Cu(II) and Ba(II) metal complexes in chloroform-d ( $\text{CDCl}_3$ ) and dimethyl sulfoxide (DMSO)-d<sub>6</sub>, using tetramethylsilane as a reference. The melting temperatures of the compounds were ascertained using a Gallenkamp device equipped with a heated stage. A TripleTOF 5600 spectrometer (SCIEX, Toronto, Canada) was utilized to analyze the mass spectra. Melting point was observed directly by using hot-stage Gallen Kamp Melting Apparatus. Percent composition of carbon, oxygen and hydrogen were determined experimentally by Liebig Method. Percent composition of nitrogen has been determined by Kjeldal's Method while Cl by Carius Method.

### Synthesis of Schiff Base and its Characterization

The synthesis of the Schiff base 4-((octadecylimino)methyl)phenol involved refluxing 30 ml of an ethanoic solution containing 4 hydroxybenzaldehyde (0.03 mol, 4.5 gm) for six hours while adding 0.03 mol of octadecyl amine (10.10 gm) and 5 ml of glacial acetic acid. After obtaining a light brown solid mass, it was first cleaned with hexane and then crystallized again using ethanol. Completion of the reaction was confirmed using TLC. Then, it was characterized for Melting point, elemental composition, molecular formula and structure.

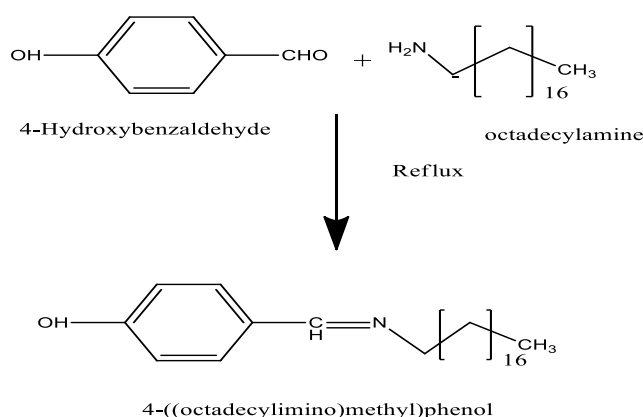


Fig 1: Scheme for Schiff Base Synthesis

### Analytical data of the synthesized compound

#### $\text{C}_{25}\text{H}_{43}\text{NO}$

Color: Light brown; yield 65%; melting point 113–114 °C; Infrared (IR) ( $\text{KBr}$ ,  $\text{cm}^{-1}$ ): 3391  $\nu(\text{O-H Phenolic})$ , 1294  $\nu(\text{C-O Phenolic})$ , 1632  $\nu(\text{HC=NH})$ . Mass Spectroscopy (MS) for  $\text{C}_{25}\text{H}_{43}\text{NO}$  ratio of mass to charge ( $m/z$ ) 373.3264;  $[\text{M}+\text{H}]^+$ : 374.3342.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz,  $\delta$ ): 6.76–7.45 (d, CH, ArH,  $J = 8.1$  Hz); 4.9 (s, 1H, OH), 0.96 (m, 3H,  $\text{CH}_3$ ), 1.33 (m, 2H,  $\text{CH}_2$ ), 1.29 (m, 2H,  $\text{CH}_2$ ), 8.39 (s, CH=N).

From the above data, the structure of prepared Schiff bases i.e. is as follows:

Analysis of Elements of Schiff base

Molecular formula of Schiff base :  $\text{C}_{25}\text{H}_{43}\text{NO}$

Molecular weight of Schiff base : 373

Melting point of Schiff base : 113–114 °C

Table 1: Elemental composition of Schiff base

	C%	H%	N%	O%
Calculated	80.42	11.52	3.75	4.30
Observed	80.37	11.54	3.70	4.35

### Synthesis and Characterization of (Cu– C<sub>50</sub>H<sub>86</sub>CuCl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>) complex

C<sub>50</sub>H<sub>86</sub>CuCl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>

30 milliliters of ethanol were used to dissolve 0.134 grams of solid copper chloride to make one millimolar of ethanolic copper chloride solution., 0.746 g solid Schiff Base was dissolved in 30 ml of ethanol to make its 2 millimolar ethanoic solution. The light green precipitates were formed by agitating these two solutions for five hours. The light green colored solid obtained was cleaned with ethanol and then crystallized again using THF. This was characterized for Melting point, elemental composition, molecular formula and structure.

### Analytical data of the synthesized metal complex

C<sub>50</sub>H<sub>86</sub>CuCl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>

Color: light green: yield: 65%, M.P: 217–219 °C, IR (KBr, cm<sup>-1</sup>): 1594  $\nu$ (-HC=N-), 1286  $\nu$ (C-O)phenolic, 484  $\nu$  (M-N), MS for C<sub>50</sub>H<sub>86</sub>CuCl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>  $m/z$ : 881.5315; [M+H]<sup>+</sup>: 882.5395.

### Analysis of Elements of Cu– Schiff base complex

Molecular formula of Cu– Schiff base complex : C<sub>50</sub>H<sub>86</sub>CuCl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>

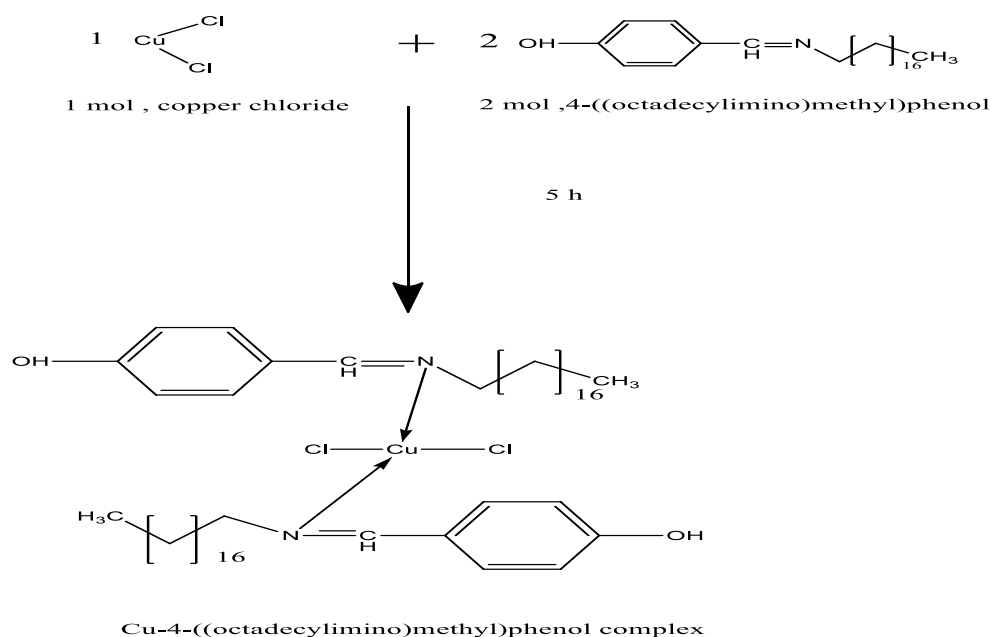
Molecular weight of Cu– Schiff base complex : 881

Melting point of Cu– Schiff base complex : 217–219 °C

Table 2 Elemental composition of Cu– metal complex

	C%	H%	N%	O%	Cl %	Cu%
Calculated	68.10	9.76	3.17	3.63	8.05	7.20
Observed	68.08	9.80	3.19	4.60	8.09	7.16

From the above data, the structure of prepared Cu–Schiff base complex is as follows:



**Fig 2: Scheme for Cu-Schiff Base Complex Synthesis**

### Synthesis and Characterization of (Ba- C<sub>50</sub>H<sub>86</sub>BaCl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>) complex

C<sub>50</sub>H<sub>86</sub>BaCl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>)

A one millimolar ethanoic solution of barium chloride was prepared by dissolving 0.208 g of solid barium chloride in 30 ml of ethanol. 0.1910 g of solid Schiff Base was dissolved in 30ml of ethanol to prepare 2millimolar solution of 4-(octadecylimino)methyl)phenol. These two solutions were agitated for five hours to produce the red precipitates. The resulting red-colored solid was recrystallized in THF after being cleaned with ethanol. This was characterized for Melting point, elemental composition, molecular formula and structure.

### Analytical data of the synthesized metal complex

(C<sub>50</sub>H<sub>86</sub>BaCl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>)

Color: Red: yield: 68%, Melting point 232–234 °C, IR (KBr, cm<sup>-1</sup>): 1584ν(-HC=N-), 1296 ν(C-O) phenolic, 492 ν (M-N), MS for C<sub>50</sub>H<sub>86</sub>BaCl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>) *m/z* : 954.5112; [M+H]<sup>+</sup> : 955.5146.

Analysis of Elements of Ba- Schiff base complex

Molecular formula of Ba- Schiff base complex : C<sub>50</sub>H<sub>86</sub>BaCl<sub>2</sub>N<sub>2</sub>O<sub>2</sub>

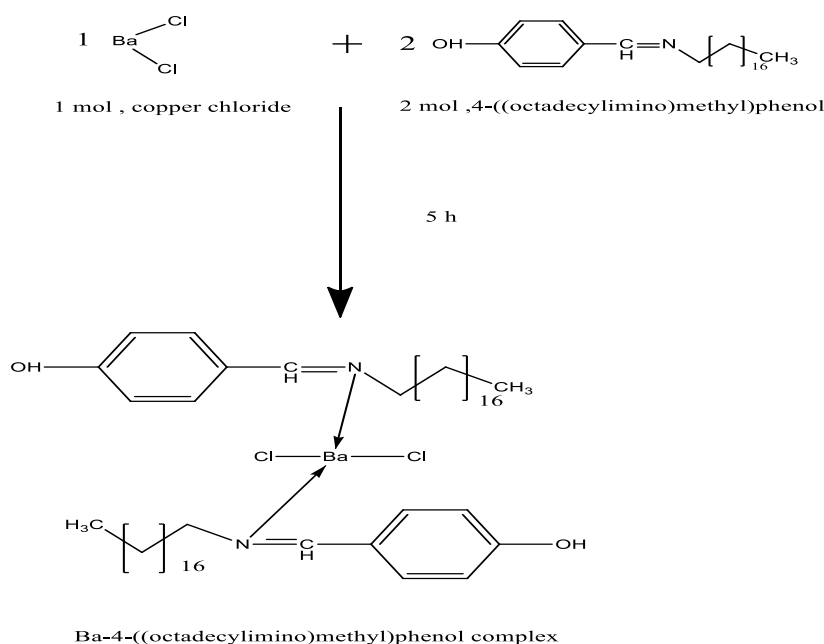
Molecular weight of Ba- Schiff base complex : 955

Melting point of Ba- Schiff base complex : 232–234°C

**Table 3 : Elemental composition of Ba- Schiff base complex**

	C%	H%	N%	O%	Ba %	Cl %
Calculated	62.85	9.07	2.93	3.35	14.37	7.42
Observed	62.80	9.10	2.95	3.40	14.40	7.37

From the above data, the structure of prepared Ba-Schiff base complex is as follows:



**Fig 3: Scheme for Ba–Schiff Base Complex Synthesis**

#### **Actions against bacteria and fungus**

*Rhizopus oryzae* (MTCC 262), *Escherichia coli* (MTCC 732), *Pseudomonas aeruginosa* (MTCC 424), *Candida albicans* (MTCC 227), *Staphylococcus aureus* (MTCC 2901), and *Bacillus subtilis* (NCIM 2063) strains used to evaluate the antibacterial and antifungal properties compounds. The serial dilution approach was used to complete this evaluation in triplicate. dimethyl sulfoxide served as the negative control, while fluconazole and ciprofloxacin were the positive controls [21,22]. To prepare stock solution, the compounds were dissolved in DMSO at a concentration of 100 µg/mL. The mixture was then serially diluted to produce concentrations ranging from 100 to 0.8 µg/ml after 1 ml of stock solutions was combined with 1 ml of nutritious broth and potato dextrose broth. Each test tube was filled with 0.1 ml of microbial suspension, and it was then incubated for 24 hours in case of bacterial and seven days in case of fungus [23,24]. The pathogens' development was visually examined in order to calculate the MIC values.

#### **Anti-inflammatory activity**

The BSA assay was used to evaluate the anti-inflammatory characteristics of Schiff Base, Cu–Schiff Base complex and Ba–Schiff Base complex. The experiment was conducted in triplicate with diclofenac sodium acting as the reference standard. Solutions with concentrations ranging from 200 to 12.5 µg/ml were prepared by dissolving the compounds in dimethyl sulfoxide (DMSO) using a phosphate buffer (0.2 M, pH 7.4). The mixture was incubated for 20 minutes at 37°C in phosphate buffer after 1 ml of BSA (1 mM) was added to each solution (4 ml) [25–27]. After the incubation, the mixtures were subjected to 15 minutes of BSA denaturation at 70°C in a water bath. After cooling, the molar absorbance at 660 nm was used to calculate the solutions' turbidity [28–30]. Percentage of denaturation in the absence of any compound served as the control.

The following formula was then used to determine the percentage of inhibition:

$$\text{Inhibition percentage} = (1 - A/B) \times 100$$

In this case, "A" stands for the control's absorbance and "B" for the compounds' absorbance. On the basis of the results on percentage inhibition, the IC<sub>50</sub> values of the substances were subsequently determined.

## Results & Discussion

### Chemistry

In this work, two metal complexes with Schiff bases (including Ba and Cu) were prepared. The substances were soluble in DMSO, THF, acetonitrile, and CDCl<sub>3</sub>, but insoluble in water. Measurement of molar conductivity indicates that the compounds exhibit non-electrolytic activity. The tetrahedral geometry and binding site via the ligand's N and Cl atoms with Metal (II) ions were validated by a number of spectrum analyses in (Fig. 2 and Fig. 3). In addition, the compounds' antibacterial, antifungal, and anti-inflammatory properties were investigated in order to assess their potential therapeutic value for use as pharmaceutical agents in the future.

### The elemental analysis

Chemical analysis (C, H, N, M) was used to determine the chemical composition and purity of the compound. **Tables 2 and 3** present the results, which clearly reveal that the chemicals are considerably pure enough to be put to use.

### Molar conductivity

The molar conductance of the compounds was determined by utilizing a  $1 \times 10^{-3}$  M dimethylformamide (DMF) solution. The generated Schiff Base and its Metal Complexes' non-electrolytic character was validated by the molar conductivity values (11–15 ohm<sup>-1</sup>cm<sup>2</sup>mol<sup>-1</sup>).

### Mass spectra

There was a strong match between the compounds' molecular mass and the molecular ion peaks ( $m/z$ ) in the mass spectra when the compounds were analyzed in acetonitrile. Because of [M+H]<sup>+</sup> ion, ligand's MS analysis revealed a molecular ion peak at  $m/z$  of 374.3342. The mass spectra of complex copper and barium showed significant peak  $m/z$  at 882.5395, 955.5146, respectively, due to the [M+H]<sup>+</sup> ion, suggesting significant compliance with mol mass. The mass spectra data collected indicated a 1:2 molar ratio of metal ions to ligands.

### NMR spectra

The complexes and their matching ligand were subjected to NMR spectrum analysis in DMSO-d<sub>6</sub> and CDCl<sub>3</sub>. The -HC=N- group in the ligand 4-((octadecylimino)methyl)phenol produced a signal in its <sup>1</sup>H NMR spectra between 8.55 – 9.42 ppm. This signal moved between 7.86 – 9.02 ppm after the metal ion was chelated, indicating that the N-atom was bonded to the metal ion. Upon complexation, the ligand's -OH signal at 9.86 ppm persisted, suggesting that it was involved in bonding with the metal ion. Additionally, minor changes in the ligand's aliphatic (1.39–4.19 ppm) and aromatic (9.20–7.35 ppm) signals confirmed that the ligands and the metal ion were chelated. The Schiff Base's azomethine carbon showed a signal in the <sup>13</sup>C NMR spectra between 158.65 – 159.28 ppm. After complexation, this signal shifted to 163.17–164.91 ppm, indicating complex formation via the -HC=N- group's N-atom. Additionally, small alterations in the aliphatic (14.98–65.22 ppm) and aromatic (109.91–148.62 ppm) signals were observed after the ligand chelated

with the metal ion, suggesting the formation of a complex. Thus, the evidence acquired indicates that the ligand is bound to the metal ion through the N-atom of the  $\text{-HC=N-}$  groups in a bidentate fashion.

### IR Spectra

By comparing the ligand's IR bands with those of the matching complexes, infrared spectroscopy was used to determine the bonding locations inside the complexes. The ligands'  $\text{-HC=N-}$  group shows a band at  $1598\text{--}1597\text{ cm}^{-1}$ , which moves to the  $1597\text{--}1591\text{ cm}^{-1}$  frequency range when it forms a bond with a metal ion, indicating complexation through the azomethine group's N-atom. The formation of new bands in the complexes, such as M–N and M–Cl at  $473\text{--}464$  and  $3459\text{--}3442\text{ cm}^{-1}$ , respectively, indicates that the ligands are attached to the metal atoms via the Cl and N atoms of the  $\text{-HC=N-}$  group. As a result, the acquired IR data supports the complex formation and is compatible with the NMR findings.

### Antibacterial and antifungal activities

In the realm of infectious diseases, the continuous evolution and adaptability of bacteria and fungi present ongoing challenges to global public health. As a result, healthcare professionals advocate for the use of antibacterial and antifungal medications to manage these ailments comprehensively. The rise of antibiotic-resistant bacterial strains underscores the urgent need for innovative antibacterial strategies. Similarly, fungal infections, which are often underestimated, are becoming increasingly significant due to the growing incidence of antifungal resistance. Thus, developing effective agents to combat these microorganisms is crucial. Using a serial dilution experiment, this study looks into the antibacterial and antifungal characteristics of Schiff base and its metal complexes in an effort to find effective medicinal medicines.

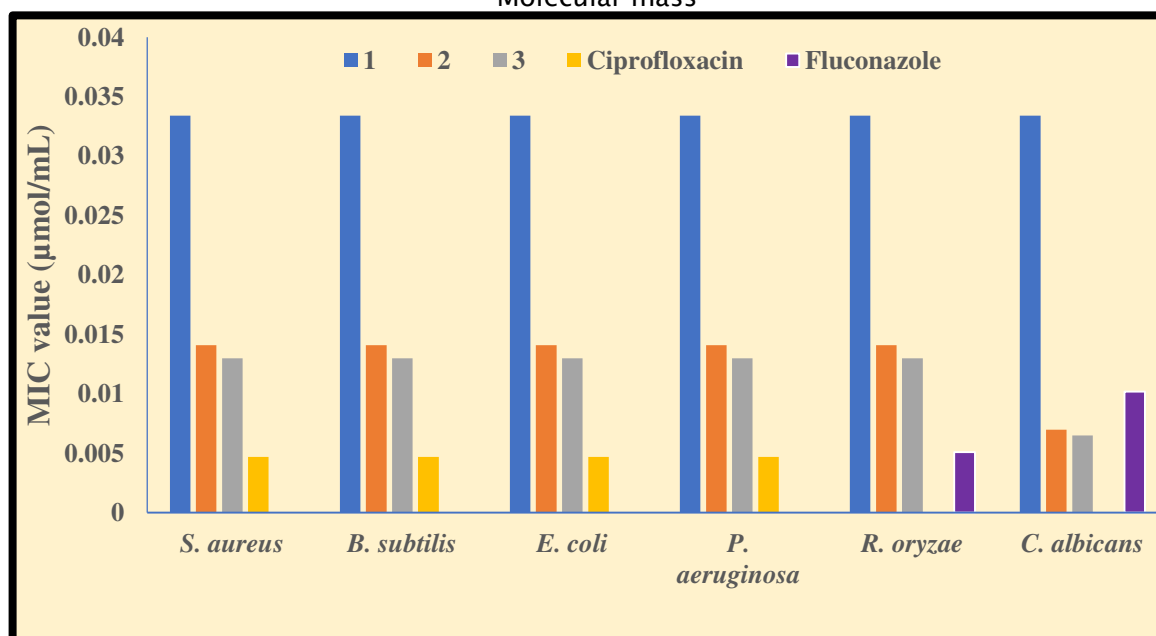
The following results are indicated by the observed activity:

1. The findings indicate that the Schiff base and its metal complexes have strong inhibitory capability against bacterial and fungal infections because of the presence of the azomethine group. With a MIC value of  $0.0334\text{ }\mu\text{mol/mL}$  for the strains tested, the Schiff base is the least active among them all [31, 32].
2. Tweedy's chelation hypothesis and Overtone's idea both explain the intriguing discovery that the complexes are more effective than the Schiff base [33, 34]. For both bacterial and fungal strains, the complexes significantly increased the inhibitory effects, which ranged from  $0.0065$  to  $0.0141\text{ }\mu\text{mol/mL}$  (Table 4 and Figure 4). Their activity in the complexes follows the order  $\text{Ba(II)} > \text{Cu(II)}$ . With the lowest recorded (MIC) values ( $0.0065\text{ -- }0.0141\text{ }\mu\text{mol/mL}$ ) and the strongest efficacy against bacterial and fungal pathogens, the Ba(II) complex is particularly noteworthy (Figure 4).
3. In summary, the Ba-Schiff base complex exhibited comparable effectiveness to ciprofloxacin and fluconazole in inhibiting bacterial and fungal proliferation across all tested strains, indicating its potential as a pharmaceutical agent. The Ba-Schiff base complex has the highest inhibition ability against *C. albicans* with  $0.0065\text{ }\mu\text{mol/mL}$  MIC value.
4. A thorough examination of the compounds investigated in this study and those mentioned in previous research [31–36] indicates that Schiff base, Cu-Schiff base complex and Ba-Schiff base complex demonstrate significant efficacy against diseases caused by both bacteria and fungi.

**Table 4. Antibacterial and antifungal activities of the compounds.**

Sr. No.	Compounds	Gram +ve bacteria		Gram -ve bacteria		Fungi	
		<i>S. aureus</i>	<i>B. subtilis</i>	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>R. oryzae</i>	<i>C. albicans</i>
1	Schiff base (373)*	0.0334	0.0334	0.0334	0.0334	0.0334	0.0334
2	Cu-Schiff base complex (882)*	0.0141	0.0141	0.0141	0.0141	0.0141	0.0070
3	Ba6-Schiff base complex (955)*	0.0130	0.0130	0.0130	0.0130	0.0130	0.0065
4	Ciprofloxacin	0.0047	0.0047	0.0047	0.0047	-	-
5	Fluconazole	-	-	-	-	0.0051	0.0102

\*Molecular mass



\*1, 2 and 3 represent Schiff base, Cu-Schiff base complex and Ba-Schiff base complex respectively.

Fig. 4. Effectiveness of the compounds against bacteria and fungi

### Anti-inflammatory activity

Inflammation emerges as a significant contributor to various serious conditions, including respiratory complications, renal dysfunction, gastrointestinal disorders, cardiac insufficiency etc. While inflammation is a vital component of the body's defense mechanism, its chronic or excessive presence poses significant risks. Prolonged inflammation is associated with various diseases, such as autoimmune effects, chronic respiratory ailments, cardiovascular conditions, and different types of cancer. With considering this, the inflammation inhibitory potential of Schiff base, Cu-Schiff base complex and Ba-Schiff base complex was assessed as part of efforts to develop therapeutic agents for inflammatory diseases.

The findings suggest the following recommendations:

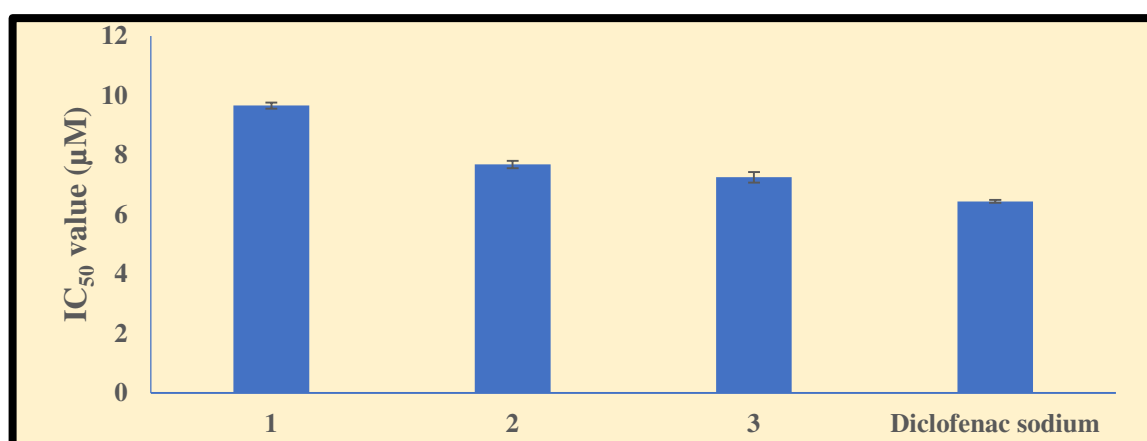
1. The investigation highlights the notable anti-inflammatory potency of all examined Schiff base, Cu-Schiff base complex and Ba-Schiff base complex, attributed to the presence of the  $\text{-HC=N-}$

group [26, 27]. Moreover, the study reveals that upon ligand chelation with metal, the inhibitory capacity of the ligand increases within the  $07.25 \pm 0.18$  to  $07.68 \pm 0.12$   $\mu\text{M}$  range (Table 5 and Figure 5). In contrast, Schiff base exhibits the least potency with an  $\text{IC}_{50}$  value of  $9.66 \pm 0.10$   $\mu\text{M}$ .

- The complexes' increased efficacy is explained by their capacity to impede protein denaturation, which is a characteristic that becomes apparent during complex formation. This inhibitory mechanism limits water retention and edema formation, thereby significantly reducing the inflammatory response [28].
- The complexes exhibit a potency trend of  $\text{Ba(II)} > \text{Cu(II)}$ , with the copper(II) complex showing the least efficacy, the Ba(II) complex exhibits the highest potency against inflammatory conditions.
- Amid the complexes, the Ba– Schiff base complex demonstrates the lowest  $\text{IC}_{50}$  value of  $07.25 \pm 0.18$  to  $07.68 \pm 0.12$   $\mu\text{M}$ , indicating the highest capacity to eliminate inflammatory conditions. The inhibitory efficacy of Ba– Schiff base complex is comparable to that of the drug diclofenac sodium, suggesting its potential for medicinal use in alleviating inflammatory effects.
- In addition, an examination of the synthesized Schiff base, Cu–Schiff base complex, and Ba–Schiff base complex in comparison to the previously published compounds [25–30] reveals a noteworthy characteristic of the created compounds: inflammation retardation.

**Table 5** Anti-inflammatory evaluation results of the synthesized compounds.

Sr. No.	Compounds	$\text{IC}_{50}$ value ( $\mu\text{M}$ )
1	Schiff base	$9.66 \pm 0.10$
2	Cu–Schiff base complex	$7.68 \pm 0.12$
3	Ba–Schiff base complex	$7.25 \pm 0.18$
4	Diclofenac sodium	$6.44 \pm 0.05$



\*1, 2 and 3 represent Schiff base, Cu–Schiff base complex and Ba–Schiff base complex respectively  
**Fig. 5.** Anti-inflammatory efficacies of the compounds

### Structure Activity Relationship (SAR)

A SAR was suggested in order to assess the impact of the metal as well as the functional groups affixed to the moiety on bioactivity as given in Fig. 1 and Fig. 2. All synthesized compounds demonstrated significant potency across various biological activities, including anti-inflammatory, antibacterial & antifungal. Publications research indicates the biological efficacy of

compound is substantially influenced by the attached group of the moiety, with the present study's activities being affected by electron-withdrawing groups, as previously reported [22–30]. The findings imply that the ligand has the least potency, and that the ligand's biological reaction is enhanced when it is chelated with a metal.

In addition, a survey of the literature shows that, in comparison to previously reported compounds, the synthesized compounds demonstrate remarkable efficacy for infectious illnesses [31–36]. The bioactivity assessments highlight that the complex Ba–Schiff base complex demonstrates the highest efficacy among the tested compounds. This superiority can be ascribed to various variables, including the stabilized aromatic ring, lipophilicity, chelating power, DNA binding efficacy, and the action of the metal.

## Conclusion

The condensation of 4-hydroxy benzaldehyde and octadecyl amine produced a novel Schiff Base. The prepared Schiff base was used to prepare complexes with Cu (II) and Ba (II) metal ions. After that they were purified by TLC and characterized for elemental analysis. It was found that the prepared Schiff Bases form complexes with both the metal ions in 1:1 and 1:2 molar ratio respectively [37]. Different analytical methods, such as NMR ( $^1\text{H}$  and  $^{13}\text{C}$ ), IR, molar conductance, elemental analysis, and mass spectrometry confirmed that the Schiff base and its metal complexes, which indicates the tetrahedral stereochemistry of the complexes via N-atom of ligands and Cl atoms. Additionally, therapeutic efficacy of prepared Schiff Bases and its metal complexes by bovine serum albumin and serial dilution techniques against bacterial, fungal, and inflammatory diseases found to be significant. It has been observed from the study that the inhibitory characteristic of Schiff Bases was improved significantly on complexation with metals. The Ba–Schiff base complex is highly effective against bacterial and fungal pathogens, as evidenced by its antibacterial and antifungal activities. Its MIC values range from 0.0065 to 0.0141  $\mu\text{mol/mL}$ , and it is particularly effective against *C. albicans*, with a MIC value of 0.0065  $\mu\text{mol/mL}$ . BSA revealed that the Ba–Schiff Base complex demonstrates the lowest  $\text{IC}_{50}$  value of  $07.25 \pm 0.18 \mu\text{M}$ , signifying its superior efficacy for inflammatory conditions. The antibacterial, antifungal and anti-inflammatory activities are well consistent with each other, stating the highest potency of Ba–Schiff base complex for use as medicinal agent.

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