

*Executive Summary of the Ph.D. Thesis entitled*

**“Mono and Binuclear Zinc (II) Complexes of  
Acyl Pyrazolone Ligands: Synthesis, Spectral  
Characterization, Crystal Structure and  
Application”**



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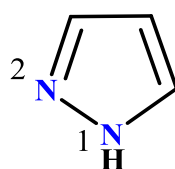
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## **Chapter 1: Introduction to Zinc(II) Complexes with Acyl- and Formyl-Pyrazolone Ligands: Pyrazolone Ligands, Zinc Choice and Applications with Emphasis on Anti-malarial Activity**

### **What is pyrazole? Why pyrazole?**

---

Pyrazole (1H-pyrazole; 1,2-diazole) (**Figure 1.1**) is a five-membered aromatic heterocyclic compound containing two adjacent nitrogen atoms in its ring. It is a stable scaffold that allows substitution at different positions, giving rise to a wide variety of derivatives with tunable electronic and biological properties. Pyrazole and its derivatives are important because they serve as versatile building blocks in medicinal, agricultural, and materials chemistry. In pharmaceuticals, pyrazole acts as a pharmacophore present in many bioactive molecules and exhibits diverse biological activities. Moreover, pyrazole-based metal complexes show enhanced biological potential, making them highly valuable in drug discovery and development.

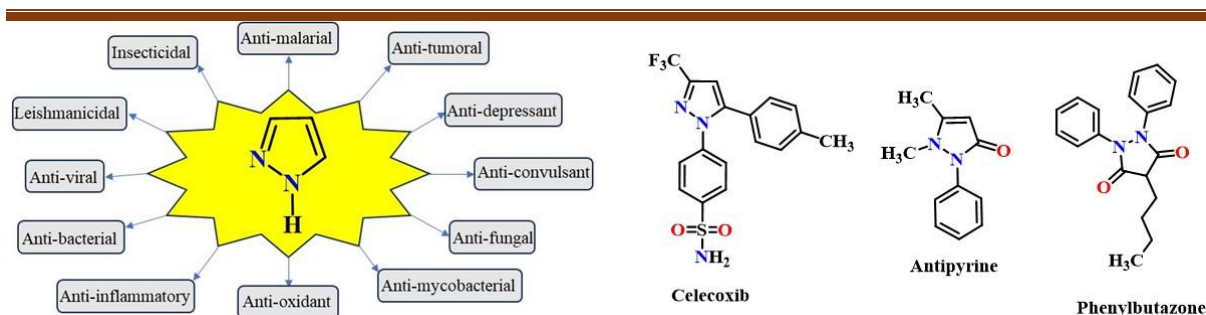


**Figure 1.1** structure of pyrazole.

### **Biological activities of pyrazole derivatives**

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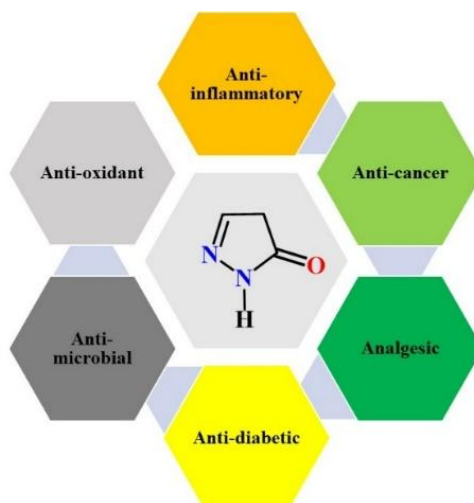
Pyrazole and its derivatives represent an important class of heterocyclic compounds exhibiting a wide spectrum of biological and pharmacological properties. The pyrazole nucleus serves as a versatile pharmacophore that has been incorporated into numerous therapeutic agents. Compounds containing this moiety have demonstrated potent anti-malarial, anti-tumoral, anti-fungal, anti-bacterial, anti-oxidant, anti-inflammatory, and anti-convulsant activities. In addition, several pyrazole derivatives exhibit anti-viral, anti-mycobacterial, Leishmanicidal, insecticidal, and anti-depressant properties. The broad range of activities associated with the pyrazole scaffold highlights its significance as a promising framework for the development of novel bioactive molecules with diverse medicinal applications [1,2]. Several pyrazole-containing drugs, including celecoxib, antipyrine, and phenylbutazone, are commercially available, with representative structures shown in **Figure 1.2**.



**Figure 1.2** Diverse biological activities associated with the pyrazole nucleus and representative pyrazole-containing drugs.

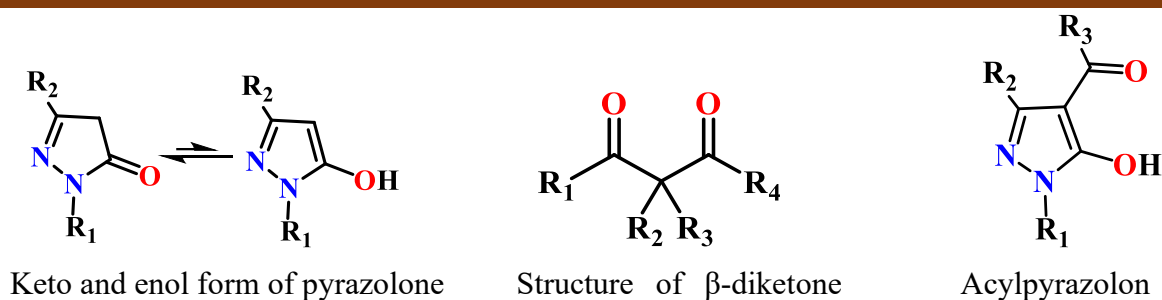
### Pyrazolone and acylpyrazolone: A special class of $\beta$ -diketones

Pyrazolones are five-membered heterocyclic compounds containing two nitrogen atoms and a keto group, typically existing in keto–enol tautomeric forms. They are important scaffolds in medicinal and coordination chemistry due to their ability to act as O, N-donor ligands (**Figure 1.3**)



**Figure 1.3** Biological applications of pyrazolone derivatives.

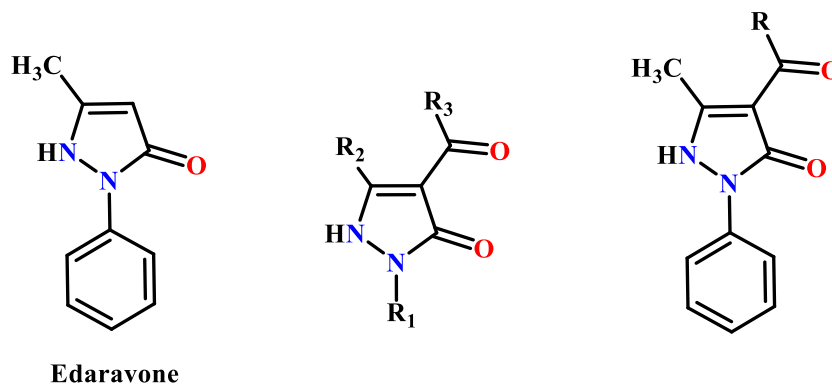
Acyl pyrazolones, particularly 4-acyl-5-pyrazolones, are a special class of  $\beta$ -diketone ligands with an acyl group at the C-4 position of the pyrazolone ring (**Figure 1.4**). This structural feature enhances their chelating ability and versatility, making them valuable in pharmaceuticals, dyes, and coordination chemistry. Jensen introduced a simple one-step synthesis, widely applied to design customized metal-coordinating ligands [3,4].



**Figure 1.4** Isomeric forms of pyrazolin-5-one and structure of acylpyrazolone.

### 4-acyl-5-pyrazolone and 4-formylpyrazolone

Edaravone (**Figure 1.5**) reacts at the C4 carbon with an acyl group to form enolizable ligands known as 4-acyl-5-pyrazolones, which act as chelating systems combining diketone coordination and biological activity from the pyrazolone ring. Similarly, 4-formylpyrazolones are structural analogues that exhibit keto–enol tautomerism. While acylpyrazolones mainly behave as β-diketone ligands, the formyl group increases electrophilicity and enables condensation with amines to produce Schiff bases. This dual-donor character expands their coordination versatility and supports the design of metal complexes with tunable structural and biological properties.

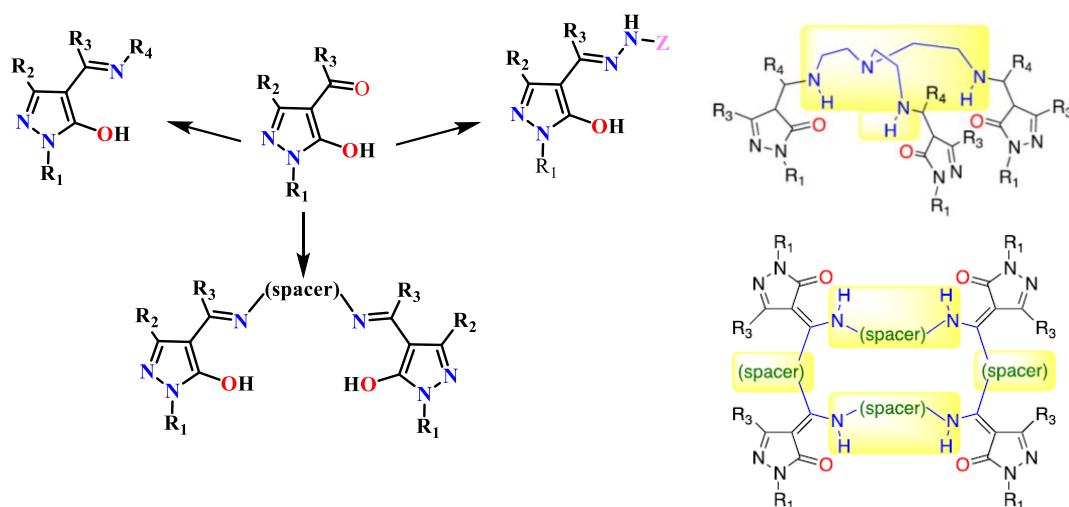


**Figure 1.5** Structure of Edaravone (3-methyl-1-phenyl-5-pyrazolone) (left) and generic structure of a 4-acyl-5-pyrazolone (middle) and acylpyrazolone starting from edaravone (4-acyl-3-methyl-1-phenyl-5-pyrazolone) (right).

### Expansibility of acylpyrazolone ligands

The expansibility (**Figure 1.6**) of Acylpyrazolones is primarily achieved through the condensation of a ketone group within pyrazolones with substituted hydrazine via a Schiff base reaction. Numerous recent studies have focused on pyrazolones, particularly those that feature

hydrazone, semicarbazone, and thiosemicarbazone functional groups. Thus far, a wide array of bidentate, tridentate, tetradentate, hexadentate, bis-, tris-, and tetrakis-5-pyrazolones have been synthesized, and their coordination chemistry extensively investigated [5].



**Figure 1.6** Bis-, tris- and tetrakis pyrazolone ligands.

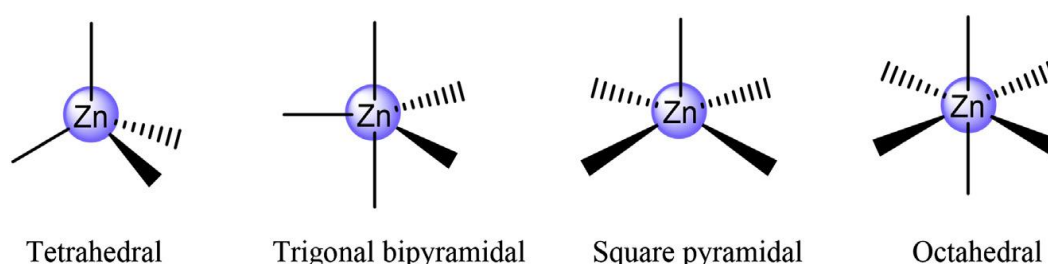
## Importance of zinc

Zinc (atomic number 30) is a bluish-white metal with a stable +2 oxidation state and an electron configuration of [Ar] 3d<sup>10</sup> 4s<sup>2</sup>. Discovered by Andreas Marggraf in 1746, it melts at 419 °C and boils at 907 °C. Zinc plays vital roles in industry, medicine, and chemistry. It is widely used for galvanization, in brass alloys, and in Zn-carbon and Zn-air batteries. In daily life, zinc is essential in dietary supplements and sunscreens, while ZnCl<sub>2</sub> serves as a catalyst in various chemical processes. Recent advances focus on ZnO nanoparticles in catalysis. However, excess zinc can cause nausea, immune suppression, and environmental pollution. In coordination chemistry, zinc exhibits various geometries (tetrahedral, octahedral, trigonal bipyramidal, and square planar) and is present in metalloenzymes like carbonic anhydrase and alcohol dehydrogenase. Zn(II) complexes with Schiff base, pyrazolone, and quinoline ligands show biological activities such as anticancer, antimicrobial, and anti-malarial effects. Additionally, luminescent Zn(II) complexes are used in sensors, OLEDs, and as catalysts in polymerization and CO<sub>2</sub> fixation reactions.

## Zinc(II) coordination complexes

Organometallics and metal-organics are two major areas that have made immense contributions to coordination chemistry. Ligands derived from heterocyclic compounds containing

heteroatoms such as N, O, S, P, and As have significantly enriched metal-organic complexes. Among them, the coordination chemistry of Zn(II) has been a subject of extensive research due to its crucial role in biological systems and its versatile applications in catalysis, material science, and medicine. In recent years, zinc complexes have gained attention in sensing studies due to their luminescent and coordination properties. They are widely applied in optoelectronic fields (OLEDs, and related devices) for detecting ions, molecules, and biological species, owing to their high sensitivity, fast response, and tunable fluorescence. The typical coordination geometries of zinc complexes (**Figure 1.7**) are tetra-coordinated tetrahedral, penta-coordinated trigonal bipyramidal, penta-coordinated square pyramidal, and hexa-coordinated octahedral [6-8].



**Figure 1.7** Geometries of Zinc complexes.

## **Zinc(II) acylpyrazolone complexes**

The coordination chemistry of zinc(II) with pyrazolone-based ligands has been extensively explored in recent years owing to their versatile structural, electronic, and biological properties. Acylpyrazolone ligands are particularly attractive due to their ability to form stable complexes with main-group, transition metals, lanthanides, and actinides, enabling diverse application. Previous studies on 4-heterocyclic acylpyrazolones and their complexes have demonstrated luminescent, electrochemical, and biological properties, with reports highlighting the influence of different ligand denticities and mixed-ligand complexes on their stability and activity. Gusev et al. reported the luminescent properties of zinc(II) complexes of 4-formylpyrazolone based azomethine ligands, showing excitation-dependent emission in solution. A novel Zn(II) complex with an ethylenediamine Schiff base was developed for high-luminescence blue fluorescent OLED applications. Other works also described the luminescent properties of Zn(II) complexes based on tetradentate N<sub>2</sub>O<sub>2</sub> donor pyrazolone Schiff bases. Fabio Marchetti et al. reported a Zn(II) complex with pyrazolone-based hydrazones that showed strong activity against *Trypanosoma brucei*, the parasite responsible for African sleeping sickness. Nevertheless, relatively few attempts have been made to explore the corresponding Zn(II)

complexes for anti-malarial activity. Fabio Marchetti *et al.*, 2005 provided a comprehensive review on acylpyrazolones, covering their synthesis, characterization, coordination chemistry with diverse metals, and their wide-ranging applications [9-12].

## **Malaria and its global health impact**

---

Malaria is a life-threatening vector-borne disease caused by *Plasmodium* parasites and transmitted by female *Anopheles* mosquitoes. Among the five human-infecting species, *P. falciparum* and *P. vivax* are the most prevalent and clinically significant. Despite global control efforts, malaria remains endemic in many countries, with Southeast Asia being highly affected. India contributes the majority of regional cases, though a significant decline in malaria incidence has been observed in recent years, aligning with the national goal of elimination by 2030.

## **Plasmodium life cycle**

---

The *Plasmodium* parasite has a complex life cycle involving humans and mosquitoes, comprising liver, blood, and mosquito stages. Sporozoites infect liver cells, releasing merozoites that invade red blood cells and cause clinical symptoms. Some parasites develop into gametocytes, which are transmitted back to mosquitoes, completing the cycle. Effective antimalarial therapy requires targeting multiple stages of parasite development.

## **Present work (novelty and objective):**

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In our laboratory, we have focused on acylpyrazolone ligands with various metals, particularly evaluating their biological and anti-malarial applications *in vitro*, and have progressed significantly in anti-malarial studies. Malaria remains one of the most serious parasitic diseases worldwide, primarily caused by *Plasmodium falciparum*, with high mortality and morbidity rates. Although classical drugs such as chloroquine and quinine have been widely used, the emergence of drug-resistant strains has created an urgent need for new anti-malarial agents. Metal-based complexes, especially Zn(II), offer promising alternatives due to their stability, biocompatibility, and potential to interfere with parasite growth pathways. As a continuation of this research, we now report a Zn(II) complex with potential anti-malarial activity, presenting its single-crystal X-ray structure, spectroscopic features (IR, UV, fluorescence), thermal stability, and electrochemical behavior, thereby highlighting its relevance in biological application [13,14].

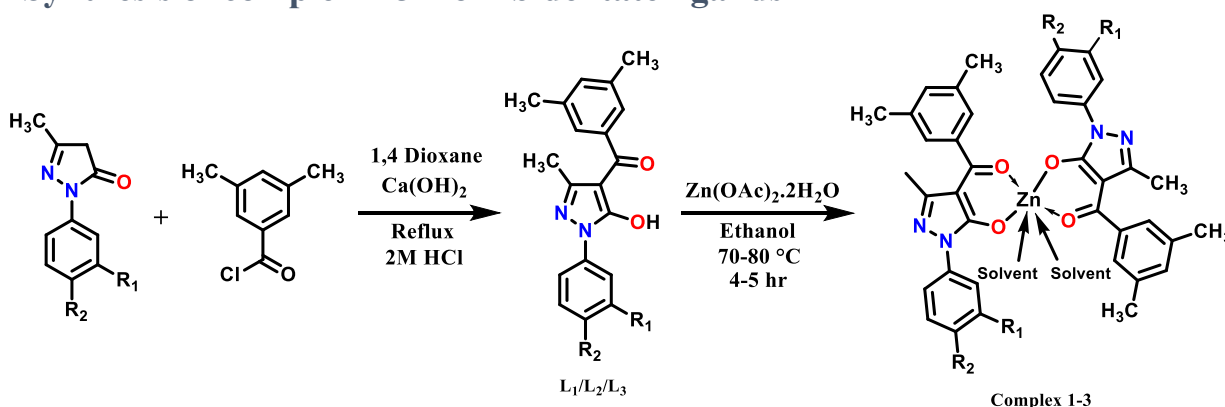
## Chapter 2: Bidentate Acylpyrazolone Zinc(II) Complexes: Synthesis, Characterization, DFT Studies, and Anti-malarial Evaluation

### Introduction

Zinc(II) acylpyrazolone complexes are important in coordination chemistry due to their structural flexibility, biocompatibility, and roles in catalysis, materials, and medicinal applications. These ligands act as O,O-bidentate donors with tunable electronic and steric properties, influencing complex stability and reactivity. This chapter reports their synthesis, structural characterization, and moderate anti-malarial activity with good biocompatibility, highlighting their potential in bioinorganic and functional materials research.

### Research Methodology (Experimental work)

#### Synthesis of complex 1-3 from bidentate ligands



**Figure 2.1** Synthesis of complexes 1-3.

The scheme outlines the synthesis of the ligands and their zinc complexes. First, a substituted pyrazolone reacts with benzoyl chloride in the presence of Ca(OH)<sub>2</sub> and 1,4-dioxane under reflux, followed by acid work-up, to afford ligands L<sub>1</sub>–L<sub>3</sub> [15]. These ligands are then treated with zinc acetate in ethanol at 70–80 °C for 4–5 h, giving zinc complexes (Complex 1–3) in 88–90% yield.

### Key Findings (Results and Discussion)

#### Elemental analysis

The elemental analysis of our zinc complexes matches very well with the theoretical values, confirming their purity (Table 2.1).

Table 2.1 Elemental data of complexes.

Code	Theoretical			Practical		
	N [%]	C [%]	H [%]	N [%]	C [%]	H [%]
Complex-1	8.29	67.21	5.07	8.30	67.53	5.04
Complex-2	7.52	61.27	4.33	7.53	61.30	4.33
Complex-3	7.96	68.23	5.44	7.96	68.25	5.76

### UV-Visible data

The complexes display a clean  $\pi \rightarrow \pi^*$  band at 270–290 nm in DMSO, and the absence of metal–ligand charge-transfer bands highlights that only the intrinsic ligand transitions are present (Figure 2.2).

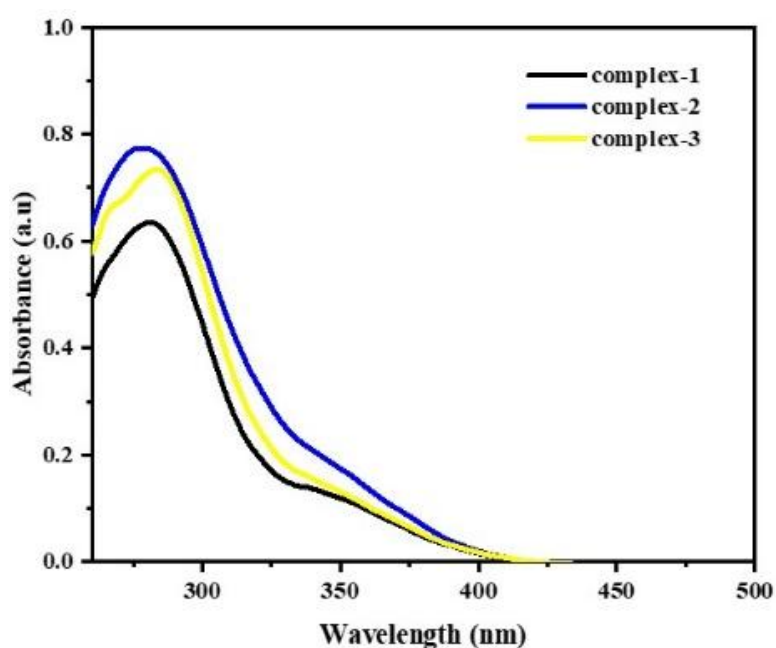


Figure 2.2 UV-Visible data of complexes 1-3.

### Other spectral data

Although complete characterization data (NMR, MS, TGA, IR, and crystallography) were obtained for all complexes, only the data for complex-1 are presented here.

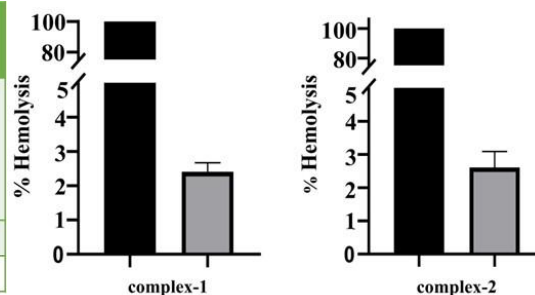


B3LYP/LanL2DZ level are presented as a representative example. Geometry optimization yielded an energy of  $-60.023$  keV, and the HOMO–LUMO energy gap was found to be  $3.90$  eV. The corresponding frontier orbital plots (HOMO and LUMO) illustrate the electron-density distribution relevant to charge-transfer processes [16].

### Anti-malarial *in vitro* and hemolytic activity

**Table 2.2** anti-malarial data of complexes.

Compound	IC <sub>50</sub> (μg/mL)	Test Condition (Reference)
L <sub>1</sub>	8.03 ± 1.18	In vitro, triplicate
L <sub>2</sub>	8.37 ± 0.89	
Complex-1	5.64 ± 1.07	
Complex-2	6.56 ± 0.29	
Quinine	0.268	S. S. Bhalodiya et al.
Chloroquine	0.02	M. Misra et al.



**Figure 2.5** Hemolytic assay of complexes 1-2.

We tested hemolysis of red blood cells with complexes 1 and 2 at  $100$  μg/mL. Both showed less than 3% hemolysis, while distilled water caused 100%. Saline was the negative control. The results are from triplicate experiments and show the complexes are safe for RBCs [17].

## Conclusion

Three Zn(II) complexes were successfully synthesized and confirmed by NMR, IR, UV-Visible, elemental analysis, TGA, mass spectrometry, SC-XRD, and PXRD, supporting their structural integrity and crystalline nature. DFT studies showed favourable HOMO-LUMO energy gaps ( $3.90$ – $3.98$  eV), optimized geometries, and global reactivity parameters, indicating electronic stability of the complexes. MEP maps highlighted electron-rich oxygen regions as nucleophilic sites, while Mulliken charge analysis confirmed Zn centres as electron-deficient and O/N atoms as donor sites. Anti-malarial evaluation against *Plasmodium falciparum* (3D7 strain) revealed moderate activity, with IC<sub>50</sub> values ranging from  $5.64 \pm 1.07$  to  $8.37 \pm 0.89$  μg/mL, lower than chloroquine and quinine standards. Hemolysis assay showed less than 3% RBC lysis at  $100$  μg/mL, confirming good biocompatibility compared to the 100% lysis of the positive control.

## Chapter 3: Tridentate 4-Acylhydrazone-5-Pyrazolone Zinc(II) Complexes: Synthesis, Characterization, DFT studies, Hirshfeld Surface Analysis and Anti-malarial Evaluation

### Introduction

Coordination chemistry plays a key role in developing bioactive molecules and functional materials. Acylpyrazolones, derived from pyrazolone frameworks, are versatile chelating ligands known for strong metal binding, Schiff base formation, and diverse pharmacological activities, including anti-inflammatory, antimicrobial, and anti-malarial effects. Zinc(II) complexes of these ligands show promising biological potential, particularly against *Plasmodium falciparum* through enzyme inhibition. This chapter describes the synthesis and crystallographic characterization of two ligands and three Zn(II) complexes and evaluates their *in vitro* anti-malarial activity using the JSB staining method, highlighting their potential as new anti-malarial agents.

### Research Methodology (Experimental work)

#### Synthesis of tridentate ligands and its complexes

##### Step-1: ligand synthesis

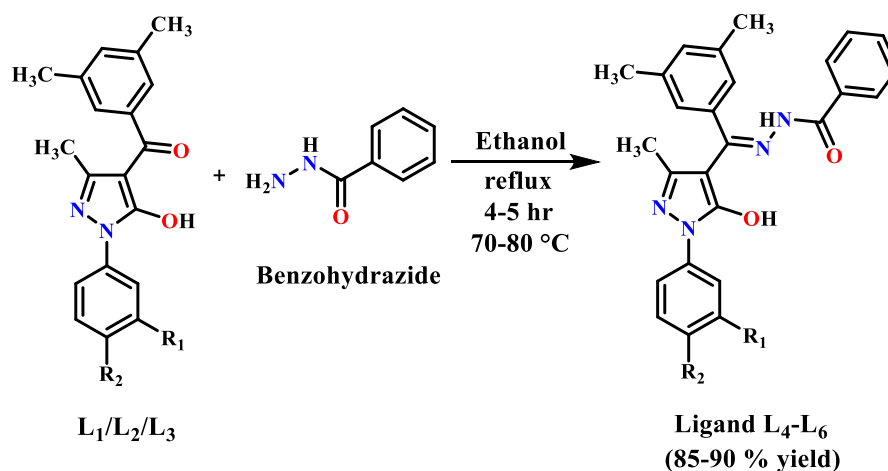
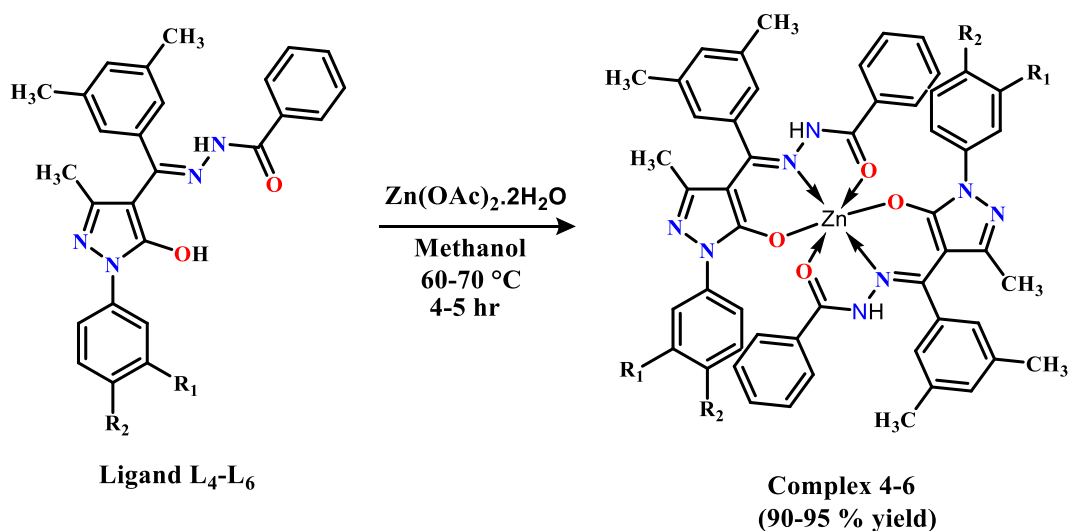
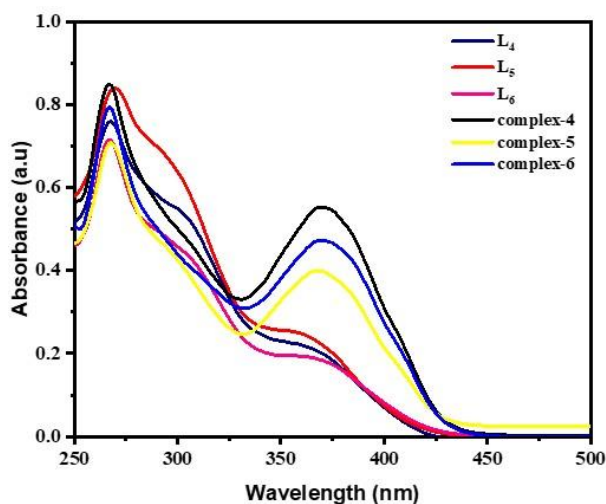
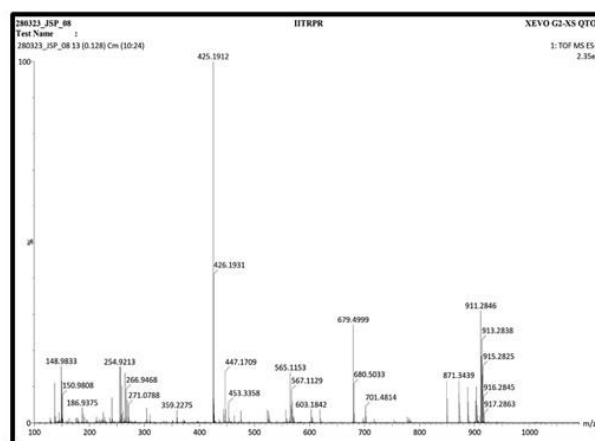


Figure 3.1 Synthesis of ligands L<sub>4</sub>-L<sub>6</sub>.

Acylated pyrazolone ligands and their Schiff base derivatives were synthesized following the reported method. The respective ligand was reacted with benzohydrazide in ethanol under reflux at 70–80 °C in the presence of a few drops of glacial acetic acid. The resulting precipitate was filtered, washed with hot ethanol, dried, and recrystallized from absolute alcohol to obtain the purified product (Figure 3.1).

**Step-2: complex synthesis****Figure 3.2** Synthesis of complex 4-6.

Zinc(II) complexes were synthesized by reacting the appropriate Schiff base ligand with zinc acetate in anhydrous ethanol under reflux. The reaction mixture was heated for several hours, leading to the formation of precipitated complexes, which were filtered, washed with cold ethanol, and dried.

**Key Findings (Results and Discussion)****Figure 3.3** UV-Visible data of ligands and complexes.**Figure 3.4** Mass spectrum of complex-4.

In DMSO, the ligands and complexes were fully soluble ( $1 \times 10^{-5}$  M) and showed UV-Visible absorption between 200–900 nm. A strong band at 260–270 nm corresponds to ligand-centered  $\pi-\pi^*$  transitions, while a band at 360–370 nm indicates metal–ligand charge transfer; d–d transitions are absent due to the  $d^{10}$  configuration.

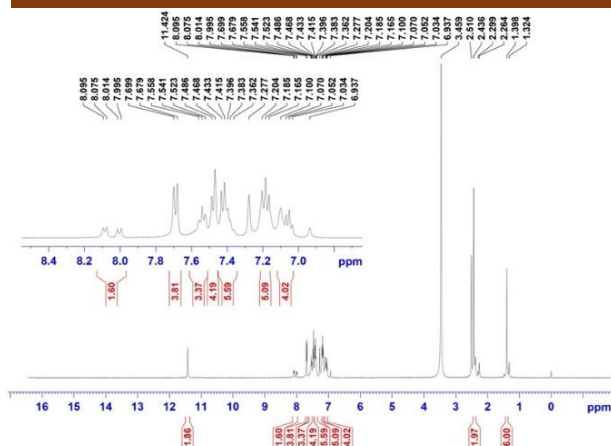


Figure 3.5 NMR of complex-4.

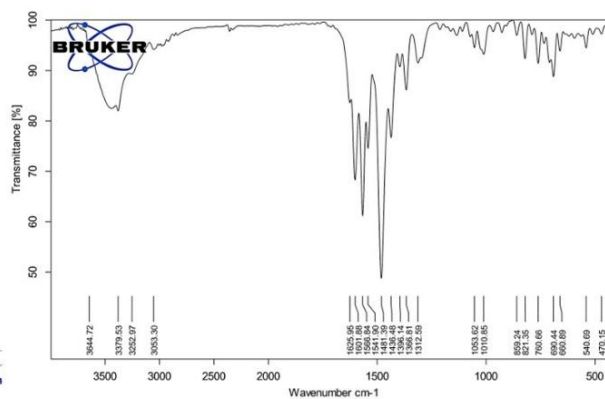


Figure 3.6 NMR of complex-4.

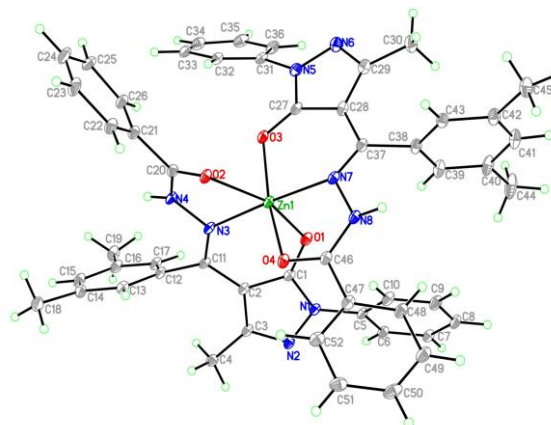


Figure 3.7 ORTEP diagram of complex-4.

## DFT computation analysis

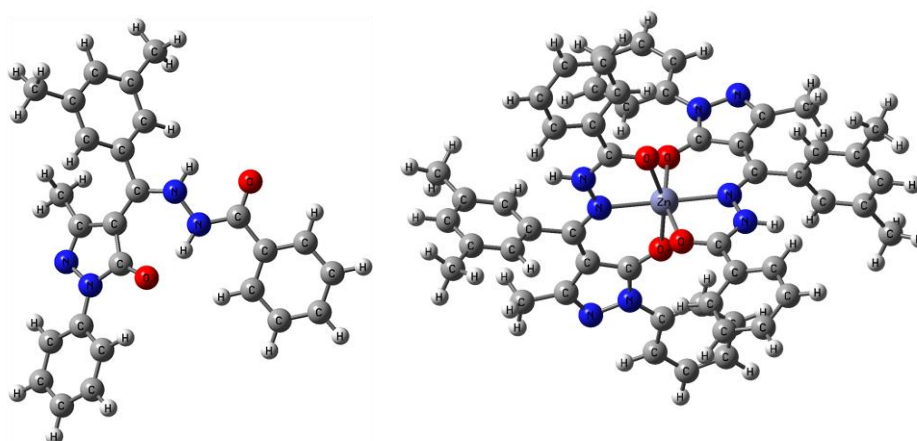


Figure 3.8 DFT optimized Geometry of L4 and complex-4 with energy value is -37.381, -76.526 keV DFT/B3LYP/6-31G/LanL2DZ.

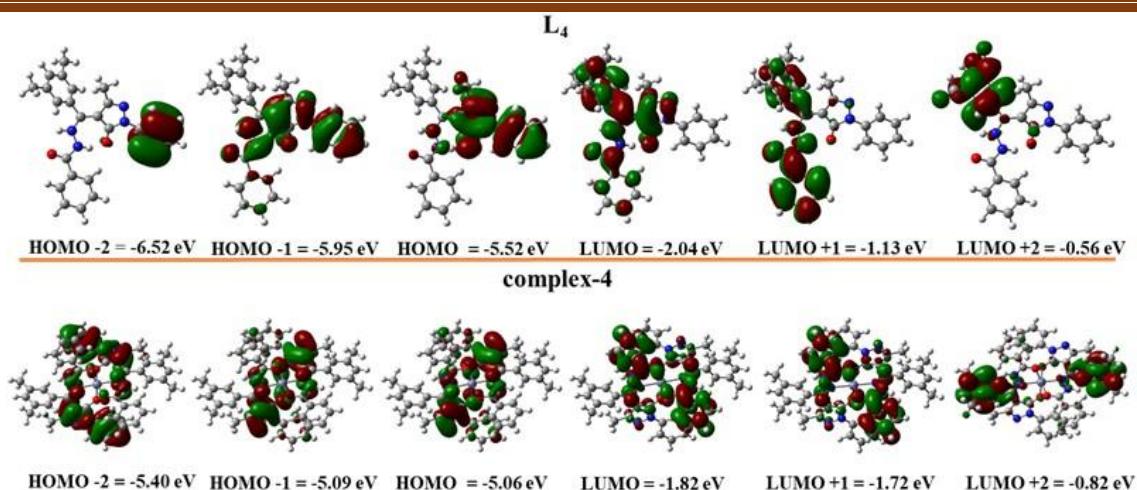


Figure 3.9 Homo-LUMO frontier orbitals of L<sub>4</sub> and complex-4.

### Anti-malarial *in vitro*

Table 3.1 anti-malarial data of complexes.

Sr. No.	Complex/Ligand	Plasmodium falciparum		Reference
		Mean IC <sub>50</sub> <sup>a</sup>		
1	Chloroquine	0.063		[14]
2	Quinine	0.826		
4	Zinc complexes 1-3 (Bidentate Mixed ligand complex)	0.11		
		0.14		
		0.95		
5	Ligands HL1-2	4.50		
		2.97		
6	Zinc complexes 1-3 (Bidentate ligand)	1.51		[20]
		2.64		
		0.81		
7	Ligands PCBPMP & PCBPMP	2.97		
		4.54		
8	L <sub>1</sub> /L <sub>4</sub> /complex-4	2.25/1.95/0.745		Present work
	L <sub>2</sub> /L <sub>2</sub> /complex-5	1.789/2.22/0.784		
	L <sub>3</sub> /L <sub>6</sub> /complex-6	1.873/1.801/0.850		

The data shown here represent the average from duplicate experimental trials. This table provides a direct comparison with compounds previously reported by our lab Metal complex substantially enhanced activity compared to ligand precursor achieving the lowest IC<sub>50</sub> value in series [14,18-20].

### Conclusion

Three tridentate Schiff base ligands and their Zn(II) complexes were synthesized and characterized by NMR, IR, UV-Visible, elemental analysis, TGA, mass spectrometry, and SC-XRD, confirming structural integrity and crystallinity. Structural studies revealed that 4-

acylhydrazone-5-pyrazolone ligands coordinate to zinc in a distorted octahedral geometry. DFT/B3LYP/6-31G/LanL2DZ studies provided insights into electronic properties, optimized geometries, and global reactivity parameters. HOMO–LUMO energy gaps (3.20–3.27 eV) indicated electronic stability and supported experimental findings. MEP maps highlighted electron-rich oxygen regions as nucleophilic sites, while Zn centres were confirmed as electron-deficient and O/N atoms as donor sites. The Hirshfeld surface analysis was also carried out to identify the crystal strength through interaction energies and energy frameworks in the ligand and intermolecular non-covalent surface interactions with fingerprint plot details in all ligands. Anti-malarial evaluation against *Plasmodium falciparum* (3D7 strain) revealed moderate activity, with IC<sub>50</sub> values ranging from 0.745 to 2.25 μM, lower than chloroquine and quinine standards.

## **Chapter 4: Quadridentate Zinc(II) Complexes from Formylpyrazolone: Synthesis, Characterization, DFT Studies and Anti-malarial Activity**

### **Introduction**

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Formyl pyrazolones are versatile β-diketone-derived ligands with strong metal-binding ability and tunable properties, capable of forming Salen/Salophen-type tetradentate Schiff bases with N<sub>2</sub>O<sub>2</sub> donor sets. Zinc(II) complexes of these systems are notable for their structural stability, photoluminescence, catalytic potential, and biological activities, including antimicrobial and DNA-interaction properties. In this chapter, five Salophen-type tetradentate ligands were synthesized from substituted formyl pyrazolones and phenylenediamine derivatives to study electronic and steric effects on coordination. Their Zn(II) complexes were spectroscopically characterized and evaluated for in vitro anti-malarial activity using the JSB staining assay.

### **Research Methodology (Experimental work)**

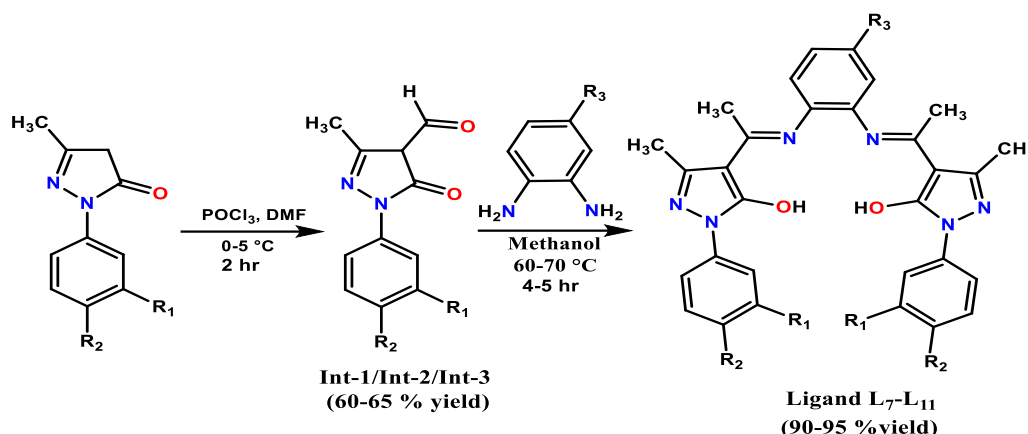
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#### **Synthesis of tetradentate ligands and its complexes**

##### **Step-1: ligand synthesis**

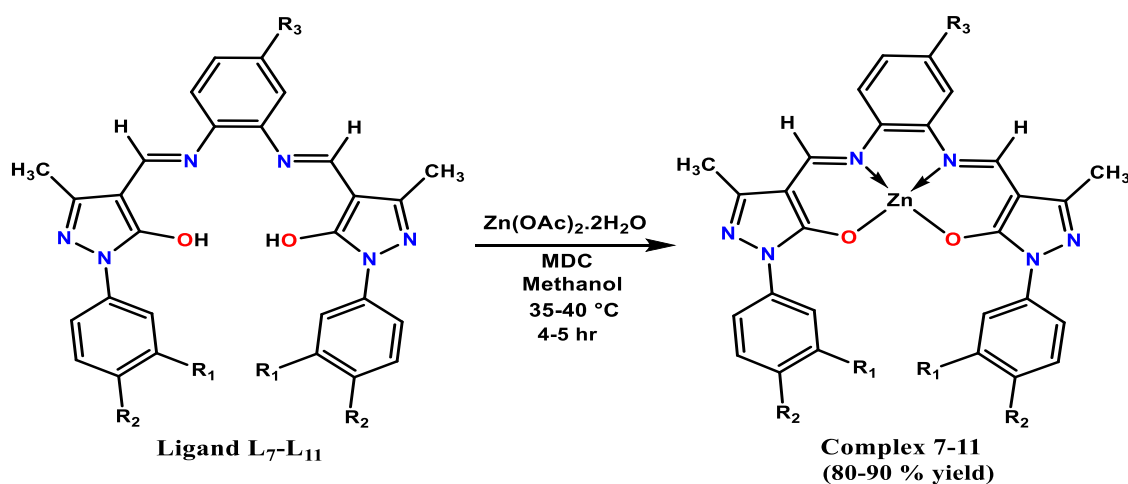
Formylated pyrazolone intermediates were prepared via a modified Vilsmeier–Haack reaction using dimethylformamide and phosphoryl chloride under controlled cooling, followed by heating, quenching in ice water, and isolation of the precipitate. The purified formylated products were then condensed with appropriate diamines in methanol under reflux to obtain

Schiff base ligands (**Figure 4.1**). The resulting products were cooled, filtered, washed with cold methanol, and oven-dried.



**Figure 4.1** Synthesis of ligands L<sub>7</sub>-L<sub>11</sub>.

### Step-2: complex synthesis



**Figure 4.2** Synthesis of complex 7-11.

Complexes were synthesized by reacting the ligands with zinc acetate in dichloromethane under reflux, followed by filtration, washing, and drying. The products were recrystallized from DMSO to obtain X-ray quality crystals and characterized by FT-IR and <sup>1</sup>H NMR spectroscopy.

## **Key Findings (Results and Discussion)**

Although complete characterization data (NMR, MS, TGA, IR, and crystallography) were obtained for all ligands and complexes, only the data for Complex-1 are presented here.

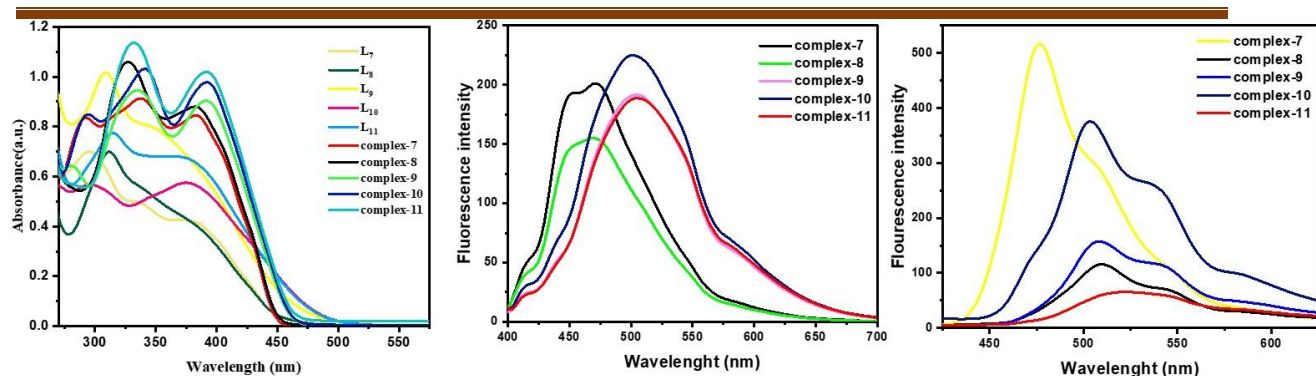


Figure 4.3 UV-Visible plot of ligands and complexes    Figure 4.4 Emission spectra in DMSO    Figure 4.5 Solid state emission spectra

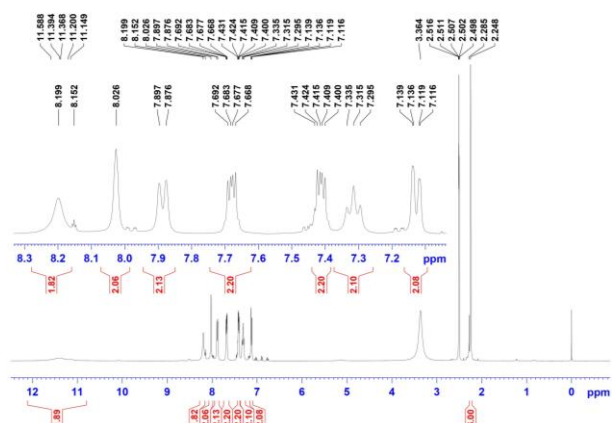


Figure 4.6 NMR of complex-7

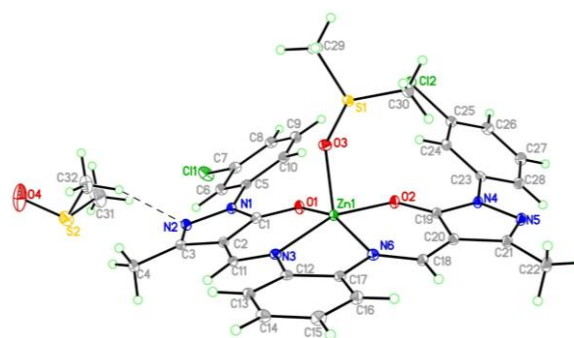


Figure 4.7 ORTEP diagram of complex-7

DFT computation analysis

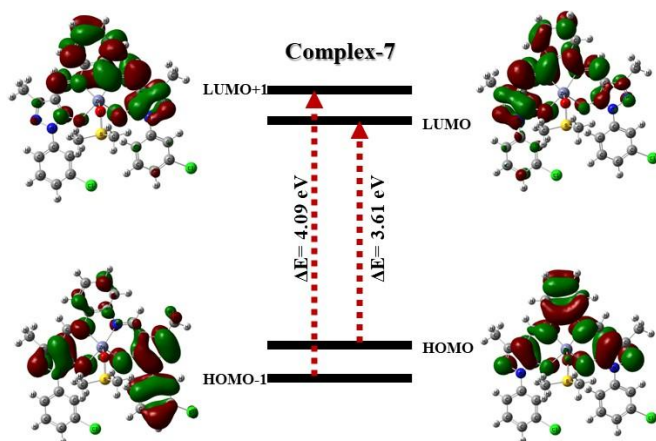


Figure 4.8 HOMO-LUMO frontier orbitals of complex-7

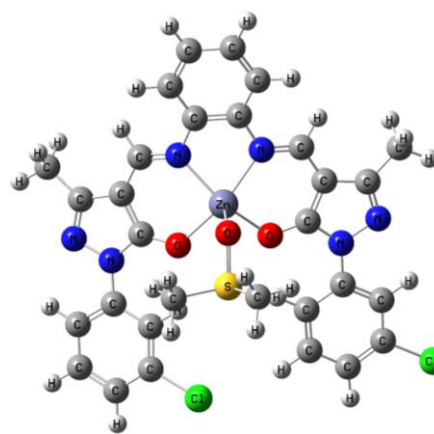


Figure 4.9 Optimized geometry of complex-7

The Density Functional Theory (DFT) study was carried out for all five complexes, and the results for complex-7 calculated at the B3LYP/LanL2DZ level are presented as a representative

example. Geometry optimization produced an energy of  $-49.460$  keV for complex-7. The HOMO–LUMO energy gaps for the entire series lie within a narrow range of  $3.53$ – $3.61$  eV, indicating that all complexes exhibit similar electronic behaviour. The HOMO and LUMO visualizations further illustrate the electron-density distribution involved in the charge-transfer process.

## Anti-malarial *in vitro*

**Table 4.1** anti-malarial data of complexes.

Sr. No.	Complex/Ligand	Composition	Plasmodium falciparum Mean IC <sub>50</sub> <sup>a</sup>	Reference
1	Chloroquine	C <sub>18</sub> H <sub>26</sub> ClN <sub>3</sub>	0.063	
2	Quinine	C <sub>20</sub> H <sub>24</sub> N <sub>2</sub> O <sub>2</sub>	0.826	
3	[Zn <sub>2</sub> (L <sub>2</sub> C) <sub>2</sub> (HQ) <sub>2</sub> ]	C <sub>57</sub> H <sub>34</sub> Cl <sub>2</sub> N <sub>8</sub> O <sub>16</sub> Zn <sub>2</sub>	0.79	[21]
4	L <sub>2</sub>	C <sub>19</sub> H <sub>17</sub> ClN <sub>2</sub> O <sub>2</sub>	1.789	[22,23] (Chapter-3)
	L <sub>3</sub>	C <sub>20</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>	1.873	
	L <sub>5</sub>	C <sub>26</sub> H <sub>23</sub> ClN <sub>4</sub> O <sub>2</sub>	2.222	
	L <sub>6</sub>	C <sub>27</sub> H <sub>26</sub> N <sub>4</sub> O <sub>2</sub>	1.801	
	Complex-5	C <sub>52</sub> H <sub>44</sub> Cl <sub>2</sub> N <sub>8</sub> O <sub>4</sub> Zn	0.784	
	Complex-6	C <sub>51</sub> H <sub>50</sub> N <sub>8</sub> O <sub>4</sub> Zn	0.850	
5	L <sub>1</sub>	C <sub>19</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	2.25	
	L <sub>4</sub>	C <sub>26</sub> H <sub>24</sub> N <sub>4</sub> O <sub>2</sub>	1.95	
	Complex-4	C <sub>52</sub> H <sub>46</sub> N <sub>8</sub> O <sub>4</sub> Zn	0.745	
6	L <sub>7</sub> /Complex-7	C <sub>28</sub> H <sub>20</sub> Cl <sub>2</sub> N <sub>6</sub> O <sub>2</sub> Zn/ C <sub>28</sub> H <sub>22</sub> Cl <sub>2</sub> N <sub>6</sub> O <sub>2</sub>	1.43/1.13	Present work
	L <sub>8</sub> /Complex-8	C <sub>30</sub> H <sub>26</sub> N <sub>6</sub> O <sub>2</sub> Zn/ C <sub>30</sub> H <sub>28</sub> N <sub>6</sub> O <sub>2</sub>	1.63/1.48	
	L <sub>9</sub> /Complex-9	C <sub>29</sub> H <sub>24</sub> N <sub>6</sub> O <sub>3</sub> Zn/ C <sub>29</sub> H <sub>26</sub> N <sub>6</sub> O <sub>3</sub>	2.13/1.51	
	L <sub>10</sub> /Complex-10	C <sub>29</sub> H <sub>22</sub> Cl <sub>2</sub> N <sub>6</sub> O <sub>3</sub> Zn/ C <sub>29</sub> H <sub>24</sub> Cl <sub>2</sub> N <sub>6</sub> O <sub>3</sub>	1.56/1.13	
	L <sub>11</sub> /Complex-11	C <sub>31</sub> H <sub>28</sub> N <sub>6</sub> O <sub>3</sub> Zn/ C <sub>31</sub> H <sub>30</sub> N <sub>6</sub> O <sub>3</sub>	1.80/1.37	

## Conclusion

In this study, five Salophen-type Zn(II) complexes (Complex-7 to Complex-11), derived from formyl pyrazolone-based Schiff base ligands, were successfully synthesized and thoroughly characterized by FT-IR, <sup>1</sup>H NMR, mass spectrometry, elemental analysis, TGA, and single-crystal X-ray diffraction, confirming their structures and N, O-chelating coordination. Structural studies revealed that the ligands coordinate to zinc in a five-coordinate distorted geometry. TGA results show that the Zn(II) complexes remain stable up to  $400$  °C, after which thermal decomposition begins. DFT/B3LYP/LanL2DZ studies provided insights into electronic properties, optimized geometries, and global reactivity parameters. HOMO–LUMO energy gaps ( $3.53$ – $3.61$  eV) indicated electronic stability and supported experimental findings. The *in vitro* anti-malarial activity of the ligands and their Zn(II) complexes was evaluated against *Plasmodium falciparum* 3D7 strain using a modified Rieckmann method and JSB staining assay. All Zn(II) complexes exhibited enhanced activity over their free ligands, with IC<sub>50</sub> values ranging from  $1.13$  to  $1.51$  μM. Complex-1 and complex-4 were the most potent (IC<sub>50</sub> =  $1.13$

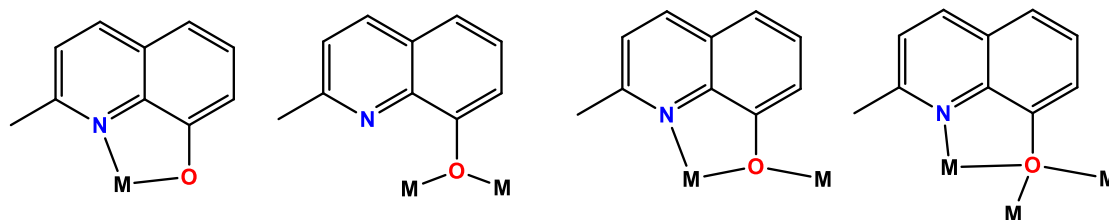
$\mu\text{M}$ ), although their efficacy remains lower than the standard drug chloroquine ( $\text{IC}_{50} = 0.063 \mu\text{M}$ ).

## **Chapter 5: Binuclear Zinc(II) Complexes: Synthesis, Characterization and Anti-malarial Evaluation**

### **Chapter 5(a): Mixed Ligand Binuclear Zinc(II) Acylpyrazolone Complexes: Synthesis, Characterization and Anti-malarial Evaluation**

#### **Introduction**

Transition metal complexes, particularly zinc(II) with pyrazolone-based ligands, are important due to their structural diversity and biological potential. Acyl pyrazolones show strong metal-binding ability and pharmacological relevance, while mixed-ligand systems with 8-hydroxyquinoline offer varied coordination modes and enhanced activity.



**Figure 5a.1** The bonding modes of HQ

This chapter reports the synthesis, crystal structure, and characterization of a binuclear zinc(II) acyl pyrazolone complex and its *in vitro* anti-malarial evaluation using the JSB staining assay. The study examines how moving from mononuclear to binuclear and mixed-ligand coordination influences anti-malarial efficacy.

#### **Research Methodology (Experimental work)**

##### **Synthesis of complexes**

In separate reaction, we take equal amounts of L<sub>12</sub>/L<sub>13</sub>/L<sub>14</sub> compound and 8-hydroxyquinoline was dissolved in methanol. After 30 min Methanolic zinc acetate solution was then added dropwise, and the mixture was refluxed for 4-5 hours. After reflux, a precipitated complex formed, which was filtered, washed with warm methanol, and dried. A small portion of the complex was collected for recrystallization, while the rest was used for further analysis and characterization.

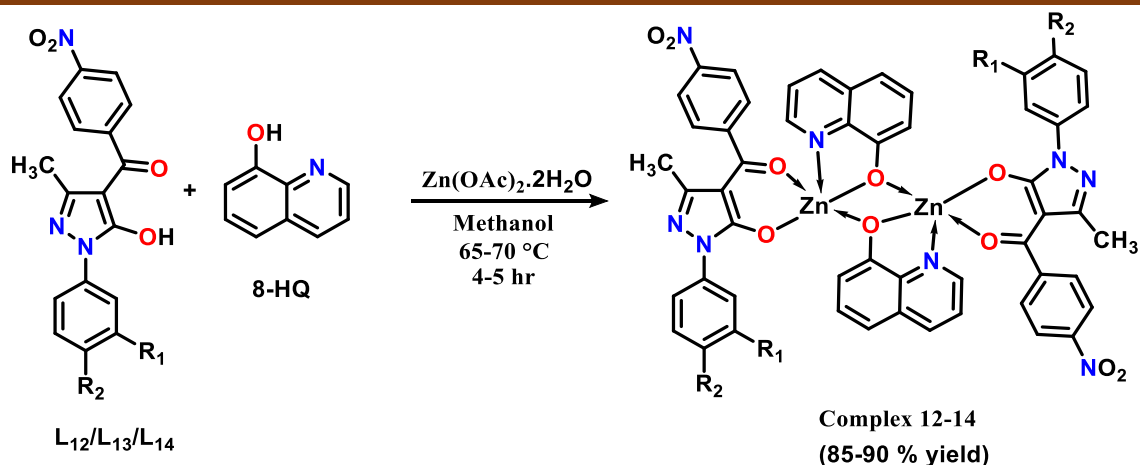


Figure 5a.2 A synthetic route of complex-12-14

In a separate reaction, equimolar amounts of the L<sub>12</sub>/L<sub>13</sub>/L<sub>14</sub> ligand and 8-hydroxyquinoline were dissolved in methanol. After stirring for 30 minutes, a methanolic solution of zinc acetate was added dropwise, and the mixture was refluxed for 4–5 hours. Upon completion, the resulting precipitated complex was filtered, washed with warm methanol, and dried. A small portion of the product was recrystallized, and the remaining material was used for further analysis and characterization.

## Key Findings (Results and Discussion)

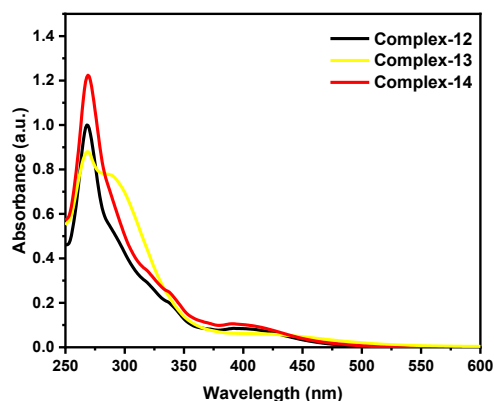


Figure 5a.3 UV-Visible plot of complexes.

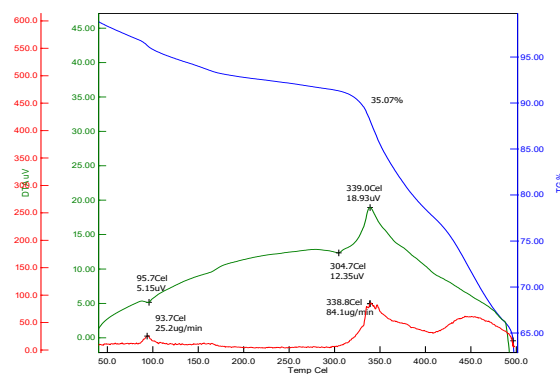


Figure 5a.4 TGA plot of complex-12.

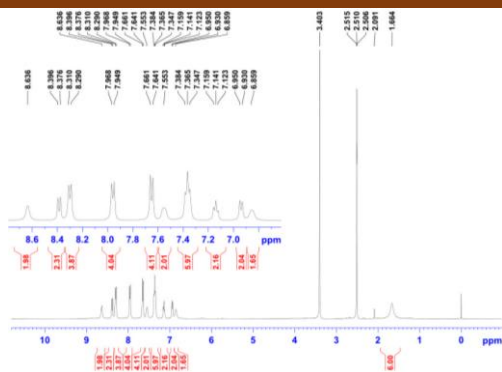


Figure 5a.5 NMR of complex-12.

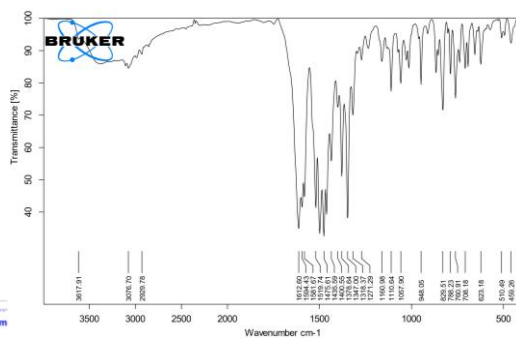


Figure 5a.6 IR of complex-12.

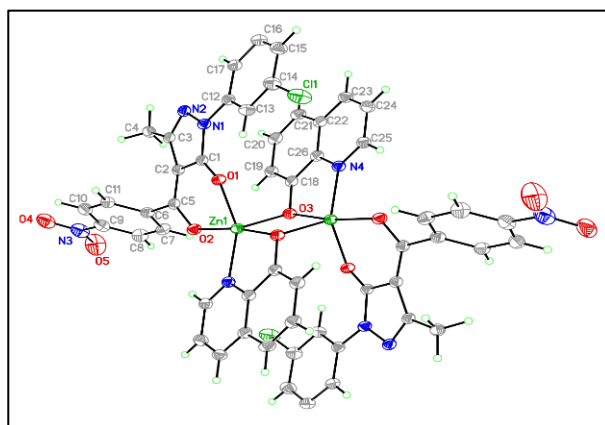


Figure 5a.7 IR of complex-13.

## DFT computation analysis

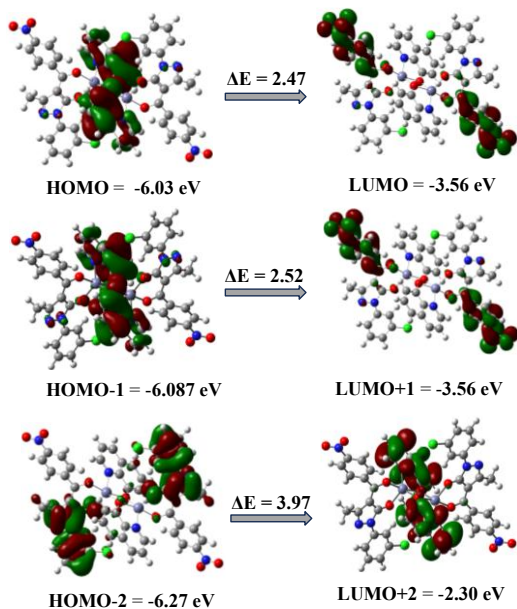


Figure 5a.8 HOMO-LUMO orbitals of complex-13.

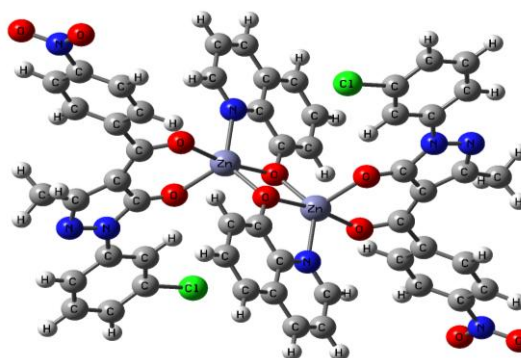


Figure 5a.9 DFT optimized geometry of complex-13.

## Hirshfeld surface analysis

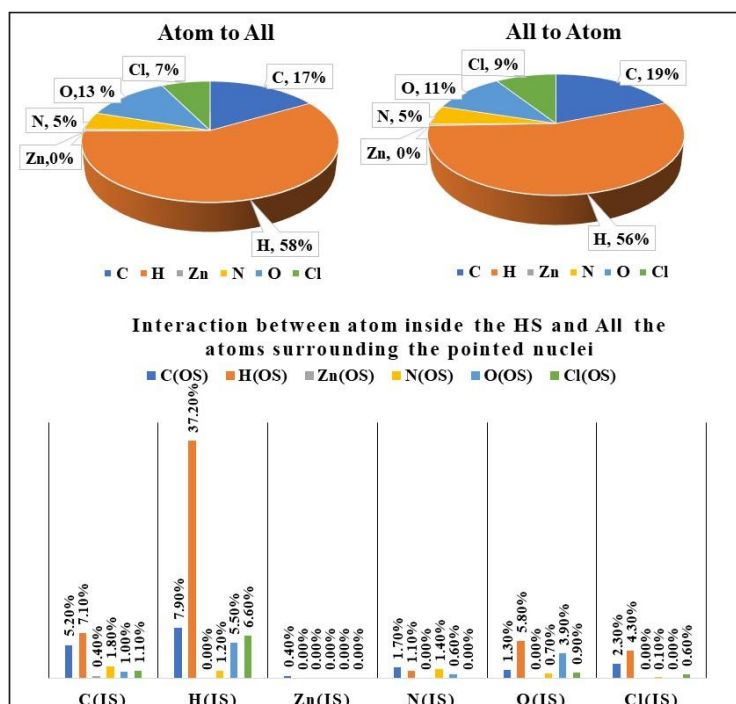


Figure 5a.10 Percentage involvement of (a) Interaction between atoms inside the HS and all the atoms located surrounding the pointed nuclei, (b) Interaction between atoms outside the HS and all the atoms located inside the pointed nuclei.

## Anti-malarial *in vitro*

Table 5a.1 anti-malarial data of complexes.

Sr. No.	Complex/Ligand	Plasmodium falciparum	
		Mean IC <sub>50</sub> <sup>a</sup>	Reference
1	Chloroquine	0.063	[14]
2	Quinine	0.826	
4	Zinc complexes 1-3 (Bidentate Mixed ligand complex)	0.11	
		0.14	
5	Ligands HL1-2	0.95	
		4.50	
6	Zinc complexes 1-3 (Bidentate ligands)	2.97	
		1.51	
		2.64	
7	Ligands PCBTPMP & PCBPMP	0.81	[20]
		2.97	
8	complex-12 L <sub>13</sub> /complex-13 complex-14	4.54	
		0.63	
		2.07/0.69	Present work
		0.76	

## **Conclusion**

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A novel mixed-ligand binuclear Zn(II) acyl pyrazolone complex was synthesized and well characterized by single-crystal XRD, various spectroscopic techniques, elemental analysis, and TGA. measurements indicated its non-electrolytic nature. DFT calculations supported the experimental findings and revealed a low HOMO–LUMO energy gap, high electrophilicity index, and negative chemical potential, reflecting good reactivity and thermodynamic stability. The complex exhibited significant anti-malarial activity *in vitro* against *P. falciparum*, suggesting its strong biological potential. Overall, the study demonstrates that such mixed-ligand zinc complexes can be promising scaffolds for further biomedical exploration and potential anti-malarial drug development.

## **Chapter 5(b): Bis-Quadridentate Ligand-Based Binuclear Zinc(II) Complexes: A Study on Synthesis, Characterization and Anti- malarial Evaluation**

### **Introduction**

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Pyrazolone derivatives are versatile building blocks in pharmaceutical and coordination chemistry, exhibiting diverse biological activities and strong metal-binding ability. Conversion of formyl-pyrazolones into Schiff bases increases denticity and enables formation of rigid Salen/Salophen-type tetradentate ligands, useful in catalysis and functional materials. Given the ongoing challenge of malaria and drug resistance, this study designs a binucleating Schiff base from formyl pyrazolone and 3,3'-diaminobenzidine and prepares its Zn(II) complexes. Zinc coordination is expected to enhance biological performance, and the resulting complexes are investigated for their anti-malarial potential.

## Research Methodology (Experimental work)

### Synthesis of binuclear bis-quadridentate complexes

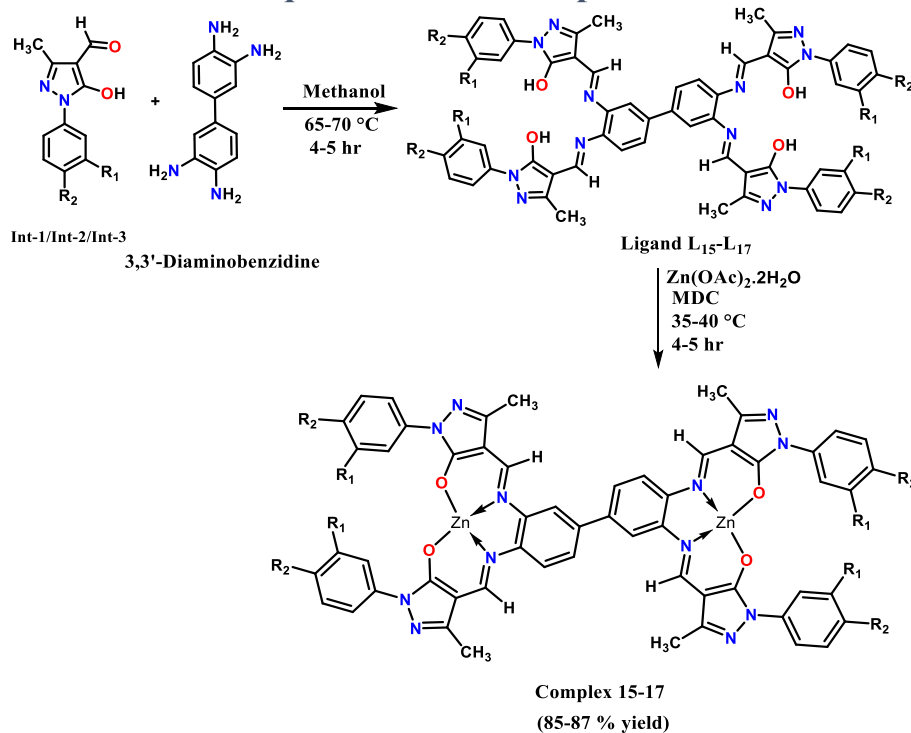


Figure 5b.1 A synthetic route of complex 15-17.

### Key Findings (Results and Discussion)

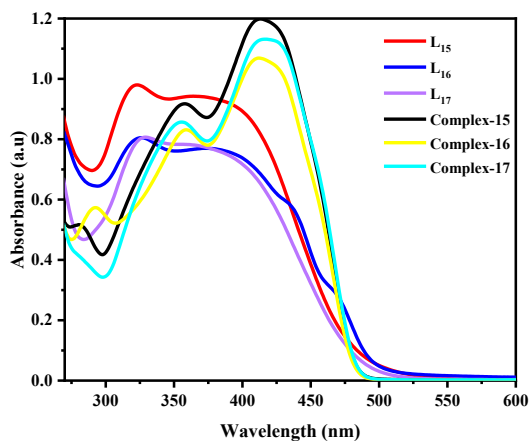


Figure 5b.2 UV-Visible plot of ligands and complexes.

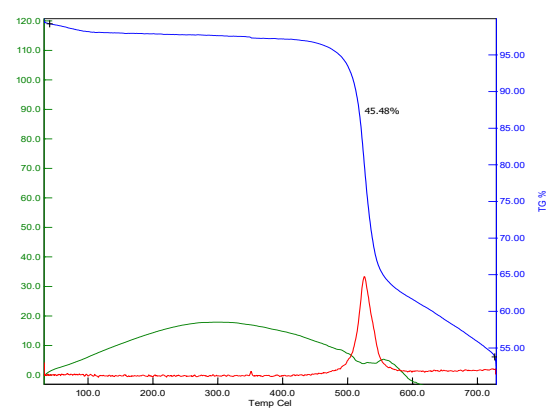


Figure 5b.3 TGA plot for complex-17.

The ligands show UV-Visible bands at 300–400 nm from intraligand transitions. In the Zn(II) complexes, a ~350 nm band arises from phenyl intraligand transitions, while the 400–450 nm band indicates MLCT or increased conjugation. All complexes show red-shifted bands

compared to free ligands, confirming electronic changes upon coordination. TGA results reveal excellent thermal stability, with no decomposition below 500 °C.

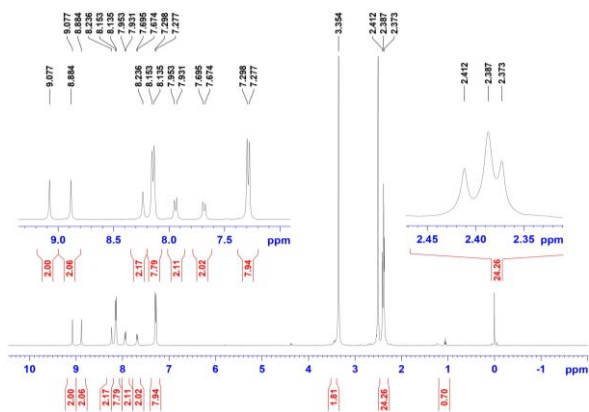


Figure 5b.4 NMR of complex-17.

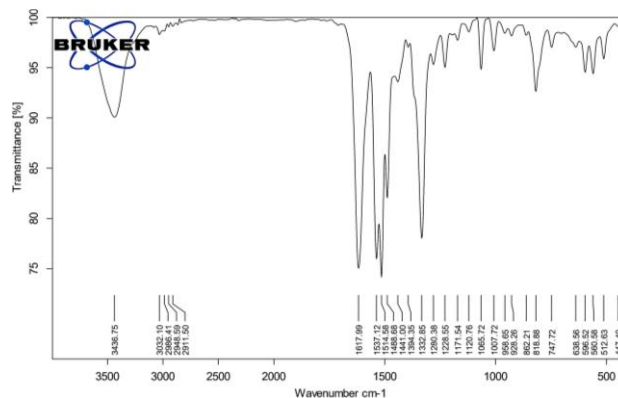


Figure 5b.5 IR of complex-17.

In the  $^1\text{H}$  NMR spectrum of complex 17, the protons of the pyrazolone methyl groups appear as two signals at  $\delta$  2.37 and 2.38 ppm. The imine protons resonate at around  $\delta$  8.9 and  $\delta$  9.0 ppm, which is in the expected downfield region. The carbonyl peak is absent in the IR spectrum, and a new C–O band appears at  $1334\text{ cm}^{-1}$ , confirming coordination.

### Anti-malarial *in vitro*

Anti-malarial activity of the developed materials in [ $\mu\text{M}$ ]

Sr. No.	Complex/Ligand	Plasmodium falciparum	
		Mean $\text{IC}_{50}^a$	Reference
1	Chloroquine	0.063	Present work
2	Quinine	0.826	
3	L <sub>15</sub>	0.69	
	Complex-15	0.67	
	L <sub>16</sub>	0.84	
	Complex-16	0.53	
	L <sub>17</sub>	0.73	
	Complex-17	0.59	

Metal complex substantially enhanced activity compared to ligand precursor achieving the lowest  $\text{IC}_{50}$  value in series. Average results of duplicate experiments.

### Conclusion

A novel binuclear bis-tetracoordinated ligands and its Zn(II) complexes was synthesized and characterized by various spectroscopic techniques, elemental analysis, and TGA, UV-Visible,

NMR, IR. The formation of the complex is confirmed by UV–Visible spectroscopy, where a distinct band appears due to metal–ligand charge transfer. All complexes show significant anti-malarial activity *in vitro* against *P. falciparum*, suggesting strong biological potential. Compared to the ligands, the complexes demonstrate improved biological activity.

### **Publications from this research**

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1. J. P. Sathvara, D. S. Sitapara, S. Ingle, R. J. Butcher, R. N. Jadeja, Bidentate Acylpyrazolone Zinc(II) Complexes: Synthesis, Characterization, DFT Studies, and Application, *Polyhedron* 282 (2025) 117765. <https://doi.org/10.1016/j.poly.2025.117765>.
2. J. P. Sathvara, R. J. Butcher, R. N. Jadeja, “Zinc(II) complexes of 4-acylhydrazone-5-pyrazolone: Synthesis, crystal structures, DFT, Hirshfeld analysis, and antimalarial potential”, *J. Mol. Struct.* 1336 (2025) 142071. <https://doi.org/10.1016/j.molstruc.2025.142071>.
3. J. P. Sathvara, R. J. Butcher, R. N. Jadeja, Design, crystallography, characterization, Hirshfeld surface analysis, and antimalarial evaluation of a zinc(II) complex with 4-acylhydrazone-5-pyrazolone: a combined DFT and experimental approach, *J. Coord. Chem.* 78 (2025) 1249-1271. <https://doi.org/10.1080/00958972.2025.2495099>.
4. J. P. Sathvara, R. J. Butcher, R. N. Jadeja, "Salophen-Type Quadridentate Zinc Complexes from Formyl Pyrazolone: Synthesis, Structure, DFT Studies, Fluorescence Emission, and Anti-malarial Activity", *J. Mol. Struct.* 1348 (2025) 143570. <https://doi.org/10.1016/j.molstruc.2025.143570>.
5. J. P. Sathvara, R. N. Jadeja, R. J. Butcher, Synthesis, characterization, and crystal features of a mixed ligand binuclear Zinc(II) acyl pyrazolone complex: DFT, Hirshfeld surface analysis and anti-malarial activity evaluation, *Inorg. Chim. Acta* 573 (2024) 122316. <https://doi.org/10.1016/j.ica.2024.122316>.
6. J. P. Sathvara, R. N. Jadeja, Novel Bis-Quadridentate Pyrazolone-Based Ligands and Zinc(II) Complexes: Spectroscopic Characterization and *In Vitro* Anti-malarial Activity, Submitted in Recent Prog. Sci. Eng. On 12<sup>th</sup> Feb 2026. (Under review)

### **References**

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- [1] Ş.G. Küçükgül et al., *Eur. J. Med. Chem.* 97 (2015) 786-815.
- [2] F. K. Keter et al., *Biometals* 25 (2012) 9-21.
- [3] M. P. Jensen et al., *J. Am. Chem. Soc.* 124 (2002) 9870–9877.
- [4] F. Marchetti et al., *Coord. Chem. Rev.* 249 (2005) 2909–2945.
- [5] F. Marchetti, et al., *Coord. Chem. Rev.* 401 (2019) 213069.

- [6] J. Tang, et al., *Inorg. & Organomet. Trans. Met. Complexes Biol. Molec. Living Cells* Academic Press, Elsevier (2017) 1–53.
- [7] F. Dumur, *Synthe. Met.* 195 (2014) 241–251.
- [8] N. Kumar, Roopa et al., *Coord. Chem. Rev.* 427 (2021) 213550.
- [9] A. Gusev et al., *J. Lumin.* 202 (2018) 370-376.
- [10] A. Gusev et al., *J. Phys. Chem. C* 123 (2019) 11850-11859.
- [11] A. Gusev et al., *Dyes Pigm.* 183 (2020) 108626.
- [12] F. Marchetti et al., *Inorg. Chem.* 61 (2022) 13561-13575.
- [13] S. Barad et al., *J. Mol. Struct.* 1294 (2023) 136345.
- [14] I. Shaikh et al., *Polyhedron* 183 (2020) 114528.
- [15] M. Travadi et al., *Polyhedron* 223 (2022) 115956.
- [16] H. Gökce et al., *J. Coord. Chem.* 72 (2019) 1075–1096.
- [17] J. E. Lazaro et al., *SLAS Discov.* 3 (1998) 49-53.
- [18] K.H. Rieckmann et al., *The Lancet* 311 (1976) 22-23.
- [19] C. Lambros et al., *J. Am. Soc. Parasitologists* 65 (1979) 418-420.
- [20] I.U. Shaikh et al., *ChemistrySelect* 4 (2019) 8286–8294.
- [21] J.P. Sathvara et al., *Inorg. Chim. Acta* 573 (2024) 122316.
- [22] J.P. Sathvara et al., *J. Mol. Struct.* 1336 (2025) 142071.
- [23] J.P. Sathvara et al., *J. Coord. Chem.* 78 (2025) 1249-1271.



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