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Biochemistry

Synthesis, Characterization of Zinc Complex and Effect of Gamma Irradiation on Biological Activities

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ABSTRACT

A new zinc(II) complex incorporating a hydrazone ligand derived from a pyran scaffold was synthesized and subjected to comprehensive physicochemical and spectral analysis. The complex exhibited a 1:1 metal-to-ligand ratio, with coordination occurring via azomethine nitrogen and carbonyl oxygen atoms, as confirmed by FT-IR, ESI-MS, UV–Vis spectroscopy, and elemental data. Thermogravimetric analysis indicated stability up to 215 °C, followed by successive decomposition stages. The biological behavior of the free ligand and its Zn(II) complex was assessed against bacterial strains and the MCF7 human breast cancer cell line. Notably, complexation with zinc enhanced both antibacterial and cytotoxic effects, which were further intensified after exposure to gamma irradiation. Structural modifications induced by irradiation were associated with improved biological responses. These findings suggest the feasibility of using radiation to fine-tune the bioactivity of metal-based therapeutic candidates, particularly those derived from hydrazone scaffolds.

Keywords: Zinc complex, hydrazone, gamma irradiation, cytotoxicity, antibacterial evaluation, thermal stability.

1. INTRODUCTION

Hydrazone derivatives are a chemically adaptable group of compounds that have demonstrated wide-ranging therapeutic applications. Their biological relevance spans various disease areas, including cancer, neurodegeneration, microbial infections, and inflammation. These molecules offer structural flexibility that facilitates derivatization and enables effective coordination with

transition metals, often resulting in complexes with improved bioactivity.

Despite considerable progress in their synthesis and structural design, the biological characterization of hydrazone-based molecules—especially in terms of molecular mechanisms—remains insufficiently explored. Among essential bioactive metals, zinc has attracted particular interest due to its central role in numerous enzymatic processes and its inherent antimicrobial and anticancer characteristics. Consequently, incorporating Zn(II) ions into hydrazone frameworks is a promising strategy for enhancing pharmacological performance.

In this study, a new Zn(II) complex formed with a pyran-containing hydrazone ligand was synthesized and thoroughly characterized through spectral, thermal, and analytical techniques. Furthermore, the biological potential of both the ligand and its metal complex was investigated before and after gamma irradiation. This approach aims to clarify how structural changes induced by irradiation influence biological behavior, thereby supporting the development of more effective metal-based therapeutic agents.

A significant family of compounds with a wide range of medicinal chemistry uses are hydrazone derivatives (Aly et al. 2021). These applications result from of extent of their pharmacokinetic properties (El-saied et al. 2020; Popiołek et al. 2018; Katariya, Shah, and Reddy 2020; Aneja et al. 2019), especially their importance in drug-identification programs(Eswaran et al. 2010; Kumar, Bawa, and Gupta 2009). Hydrazone and carbamazehyde derivatives have shown diverse biological activities, including antimycobacterial, anticancer, and anti-Alzheimer's effects (Parveen et al., 2018; Zülfikaroğlu et al., 2020; Mandewale et al., 2017; Özbek et al., 2019; Haghighijoo et al., 2017). A pyran-based hydrazone ligand has also been used to synthesize various metal complexes (Elganzory et al., 2022b). Zinc, the second most abundant trace element in the human body, plays essential biological roles and exhibits antimicrobial and antiviral activity (Crichton, 2012; Osredkar & Sustar, 2011; Castillo et al., 2016). The present study focuses on the synthesis, characterization, and biological evaluation of a Zn(II) complex with a hydrazone ligand, including the effects of gamma irradiation.

This study focuses on the development of a novel Zn(II) coordination complex derived from a pyran-based hydrazone ligand. The complex undergoes comprehensive structural and spectroscopic analyses to verify its formation and coordination pattern. Additionally, its thermal properties and biological activities—particularly antibacterial and anticancer effects—are evaluated. A central objective is to investigate the impact of gamma irradiation on both the structure and biological efficacy of the ligand and its complex, aiming to clarify how such treatment may influence therapeutic behavior.

2. MATERIAL AND METHODES

The materials, tools and techniques for applying and verifying structural integrity are covered in great depth in the supplemental file (Section S1), antimicrobial process (Section S2), cytotoxicity Assays (Section S3) (Hare 1968; Aly et al. 2023; Abdalla et al. 2020).

2.1. Synthesis of Compound

Zn^{2+} complex was prepared by magnetically stirring a solution of 0.002 moles of $ZnCl_2$. $2H_2O$ in ethanol for five to nine hours while adding 0.002 moles of the relevant ligands to 50 milliliters of EtOH (Abo-Rehab et al. ; Abdalla and Abd-Allah 2022). The resultant particles were removed by filtering, repeatedly cleaned with EtOH, and vacuum-dried on P_4O_{10}

Key analytical methods such as molar conductivity, FT-IR, ESI-MS, TGA, and antibacterial

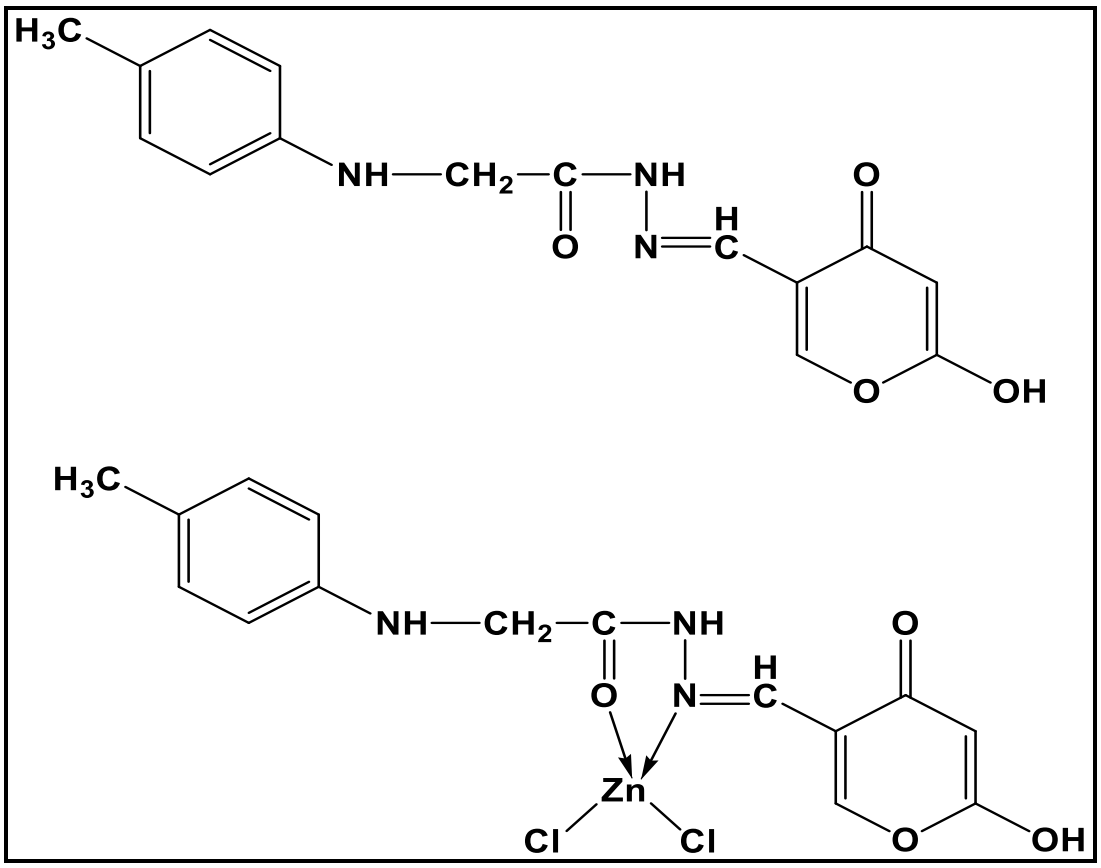

Figure. 1: Proposed structures of Compounds

2.2. Physical measurements

To investigate the B ligand and its metal complexes (B1–B4) both prior to and following irradiation, a range of spectroscopic and analytical techniques were utilized. Elemental analyses for carbon, hydrogen, chlorine, and nitrogen were performed to verify the chemical composition. The metal content was quantified through standard complexometric titration using EDTA. Mass spectrometric data for B and its complexes were obtained using a Shimadzu-QP 2010 Plus instrument.

Solid-state FTIR spectra of B and its complexes (B1–B4) were recorded with a Nenexeus-Nicolidite 640-MSA FT-IR spectrophotometer, spanning 3999–399 cm^{-1} using KBr pellet method. UV–Visible absorption spectra were measured in DMF using a Perkin Elmer Lambda 330 spectrophotometer, employing 1 cm quartz cuvettes.

Furthermore, the molar conductivity of the B1–B4 complexes in 10^{-3} M DMF solutions was evaluated using a Tacussel CD6N conductivity meter.

2.3. FT-IR spectra

The infrared spectra of the ligand and its Zn(II) complex were recorded in the range of 4000–400 cm^{-1} using a Nicolet 640-MSA FT-IR spectrophotometer. Samples (~1–2 mg) were finely ground with spectroscopic-grade KBr (~100–200 mg) to prepare transparent pellets using a hydraulic press under vacuum. KBr was pre-dried at 110 °C to eliminate moisture interference. Background correction was performed using a blank KBr disc. The spectra were used to identify characteristic functional groups and monitor coordination shifts upon complex formation.

2.4. ESI-MS spectra

The electrospray ionization mass spectra (ESI-MS) of the ligand and Zn(II) complex were obtained using a Shimadzu QP-2010 Plus mass spectrometer. Samples were dissolved in suitable volatile solvents (e.g., methanol) and introduced into the instrument via direct infusion. The spectra were recorded in positive ion mode to determine the molecular ion peaks and confirm the proposed molecular structures of the synthesized compounds. Accurate mass measurements supported the stoichiometric assignment of the complex and the integrity of the ligand.

2.5. Thermogravimetric Analysis (TGA)

Thermal stability and decomposition behavior of the Zn(II) complex were investigated using thermogravimetric analysis. The measurement was performed under a nitrogen atmosphere using a heating rate of 10 °C/min from room temperature up to 800 °C. Approximately 5–10 mg of the complex was placed in a platinum crucible. The TGA curve was recorded using a calibrated thermal analyzer, and the data were used to evaluate decomposition steps, estimate mass losses, and identify possible fragments associated with each thermal even

2.6. Antibacterial Bioassay

The antibacterial activity of the ligand and its Zn(II) complex, before and after gamma irradiation, was evaluated using the agar well diffusion method. Test organisms included selected Gram-positive and Gram-negative bacterial strains. Nutrient agar plates were inoculated with standardized bacterial suspensions (approximately 10^6 CFU/mL), and wells (6 mm in diameter) were filled with 100 µL of compound solutions at a concentration of 10 mg/mL. Plates were incubated at 37 °C for 24 hours, and zones of inhibition were measured in millimeters. Gentamicin and ampicillin served as reference antibiotics for comparison.

2.7. Cytotoxicity Assay (MTT Method)

The cytotoxic effect of the synthesized compounds was assessed using the MTT assay against the human breast cancer cell line MCF7. Cells were seeded into 96-well microplates at a density of 1×10^4 cells/well and incubated for 24 hours at 37 °C in a humidified atmosphere with 5% CO_2. The tested compounds were added at various concentrations (31.25 to 1000 µg/mL) and incubated for an additional 48 hours. After treatment, 20 µL of MTT solution (5 mg/mL in PBS) was added to each well and incubated for 4 hours. The resulting formazan crystals were solubilized with DMSO, and absorbance was measured at 570 nm using a microplate reader. IC_{50} values were calculated using non-linear regression analysis.

3. RESULTS and DISCUSSION

3.1. The physical-chemical characteristics

The color of Zn(II) complex does not change when exposed to air or moisture. The complex's analytical results are in agreement with the suggested formulae for molecules and validate the formation of 1:1 (M:L) complex, structures 1. Molar conductivity value of Zn(II) complex was 10 $\Omega^{-1}cm^2mol^{-1}$ in DMF solution. Their complex values show that there is no electrolysis involved (Nunes et al. 2020; Sardaru et al. 2021).

Table 1. Analytical data of the compounds.

Compounds	Color Yield %	Molecular weight	Conductivity µs	Found (cal.) %			
				C	H	N	M
Ligand $C_{15}H_{15}N_3O_4$	Beige 84	301.30	-	59.53 (59.80)	5.09 (5.02)	13.46 (13.95)	-
Zn(II) complex $C_{15}H_{15}Cl_2N_3O_4Zn$	Yellow 75	437.58	10	41.09 (41.17)	3.51 (3.46)	9.52 (9.60)	14.83 (14.94)

3.2. FT-IR spectra of ligand and Zinc (II) complex

The IR spectrum of the ligand showed bands at 3100, 1716, and 1573 cm^{-1} corresponding to N–H, C=O, and C=N groups. In the Zn^{2+} complex, these bands shifted to 3215, 1672, and 1571 cm^{-1}, indicating coordination through C=O and C=N. New bands at 527 and 454 cm^{-1}, attributed to M–O and M–N vibrations, further support metal chelation (Alshater et al., 2023; Abdel-Rahman et al., 2023; Abo-Rehab et al., 2024).

The involvement of azomethine nitrogen and carbonyl oxygen in metal chelation was confirmed by the formation of a six-membered ring with the carbaldehyde moiety (Gaber et al., 2019; Elganzory et al., 2022a; Aly et al., 2024; Abo-Rehab et al., 2024).

Table 2. FT-IR spectral values for Compounds.

Compounds	υ(OH)/H_2O	υ(N-H)	υ (C=O)	υ (C=N)	υ (M-O)	υ (M-N)
Ligand	3357	3100	1716	1573	-	-
Zn(II) complex	3370	3215	1672	1571	527	454

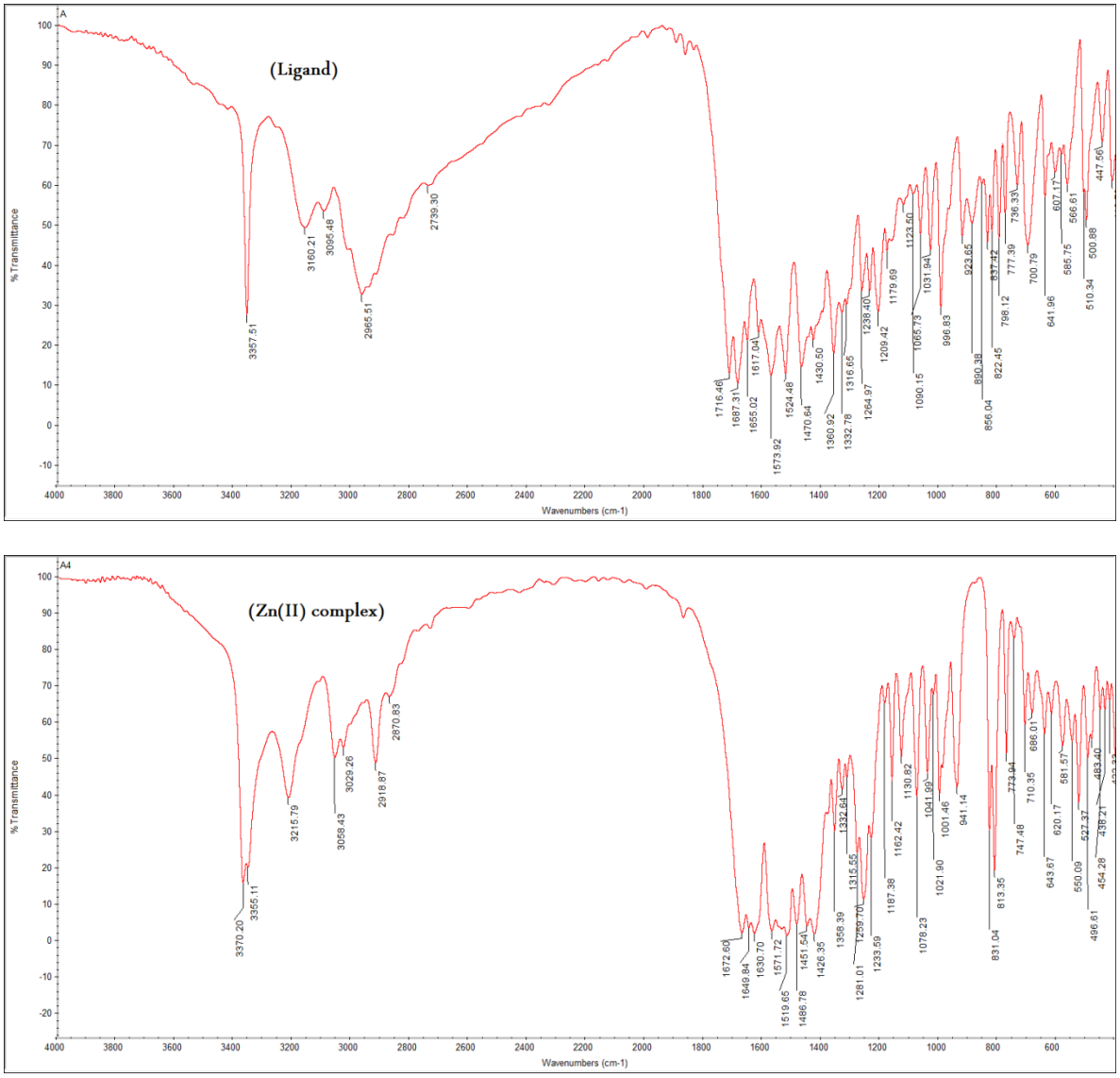

Figure. 2: FT-IR spectrum of ligand and Zn (II) complexes

3.3. ESI-MS spectra

The mass spectra of Zn(II) complex show molecular peaks at 437.61 amu. The hypothesized chemical formulae for Zn(II) complexes agree well with these findings (Figure 3).

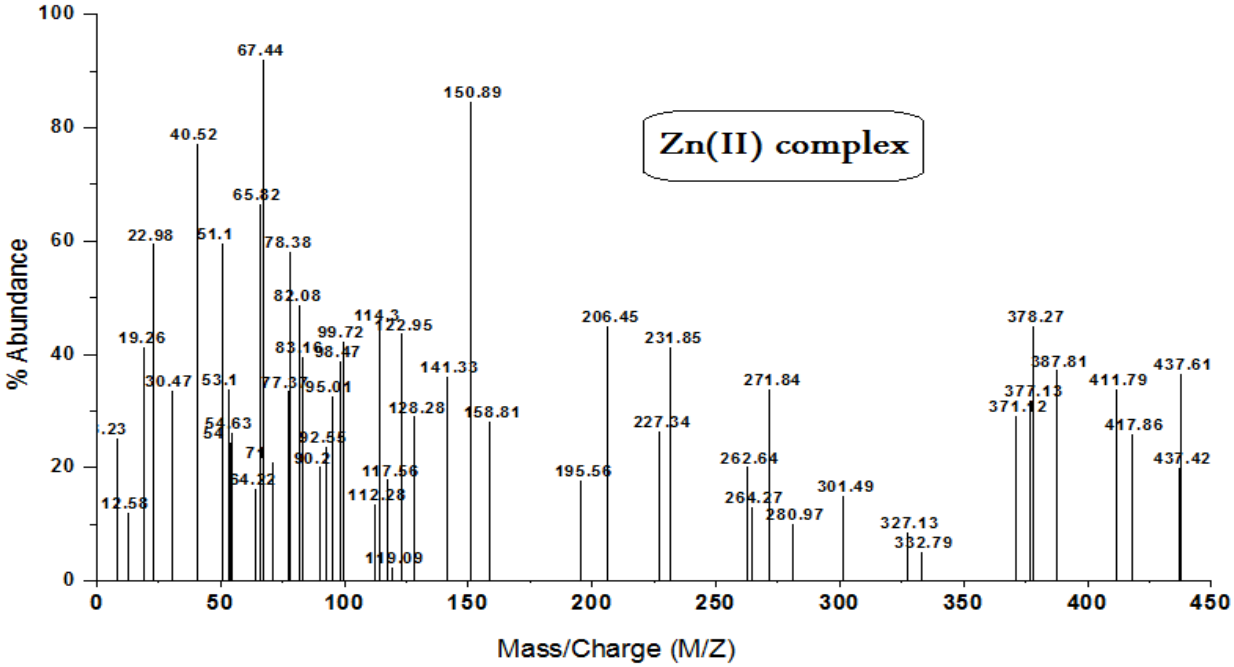

Figure 3. Mass spectra of ligand and Zn (II) complexes.

3.4. Thermogravimetric analysis

Table 3 and Figure 3 illustrates the thermal stability pattern of the synthesized Zinc chelate (TGA curve) that was obtained in a nitrogen environment, with a heating rate of 10 ^{o}C min/1 from ambient temperature to 800 ^{o}C. Note that the complex is stable up to temperature 215 ^{o}C, after this temperature the biggest fragment of the organic ligand ($C_7H_7Cl_2$) broke down in a rapid step at 352 ^{o}C. At 480.7 ^{o}C, The breakdown of the $C_2H_4N_3O$ moiety takes place in the second step, which is between 352 and 567 °C, the anticipated weight loss range for this phase is (Calc. /Found %;19.66 (19.89)). The projected mass reduction for the third stage, which occurs between 567 and 640 °C, is 28.36 (28.21) (Calc. /Found %), is thought to represent the full breakdown of the $C_7H_4N_2S$ moiety, leaving Zinc metal as the final residue.

Table 3. Thermal values of the Zn(II) complex

Compound	**TAG(A)/^{o}C**	**Wt. loss(Calc.) Found %**	**Leaving species**
Zn(II) complex	215-352	37.05 (37.45)	$C_7H_7Cl_2$
	352-567	19.66 (19.89)	$C_2H_4N_3O$
	567-640	28.36 (28.21)	$C_6H_4O_3$
Residue	>640	14.94 (14.43)	Zn

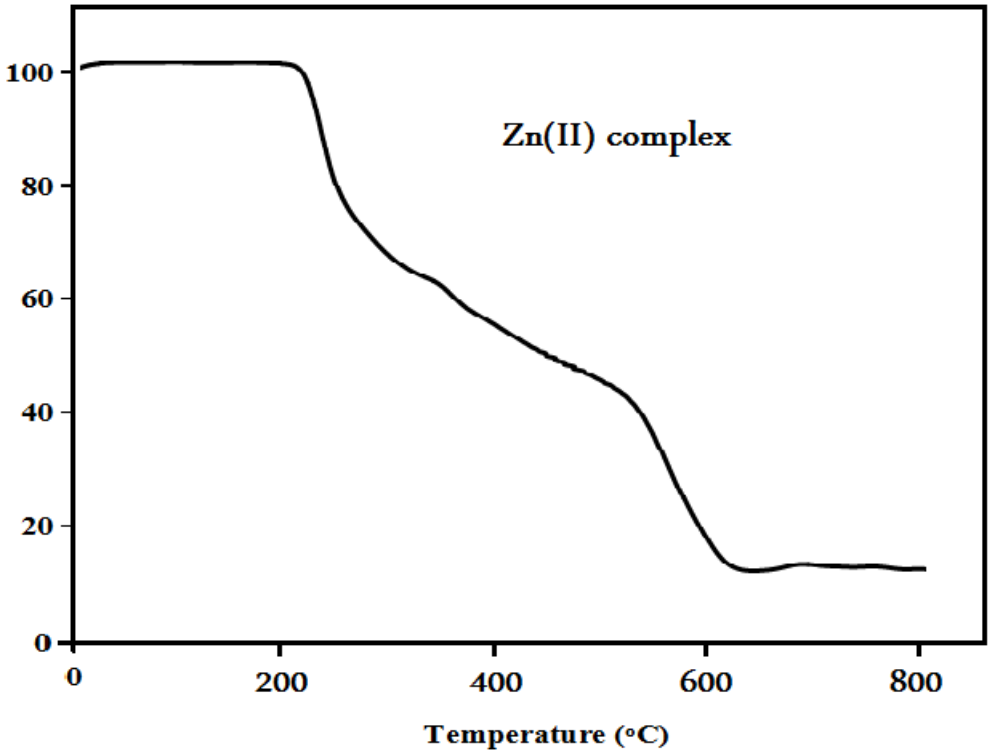

Figure 3. TGA curves for the Zn(II) complex.

3.5. Antibacterial bioassay

Certain pharmaceuticals show greater efficacy against Gram-positive than Gram-negative bacteria. In this study, the antibacterial activity of the ligand and Zn(II) complex, before and after irradiation, was evaluated using the agar diffusion method (Hassan et al., 2024).

Table S1 and Figure 4 present a list of the measured bactericidal activity of ligand and Zn(II) complex (Reedijk and Bouwman 1999). When the ligand chelated with Zn (II) to form complex, An increase in the ligand's antibacterial activity was observed, further enhanced upon Zn(II) complexation due to partial charge sharing with donor atoms (N and O), leading to electron delocalization within the chelate ring. Factors such as geometry, donor type, metal ion, overall charge, and chelation contribute to biological activity (Ispir, 2009). Notably, the irradiated Zn(II) complex showed strong antibacterial effects.

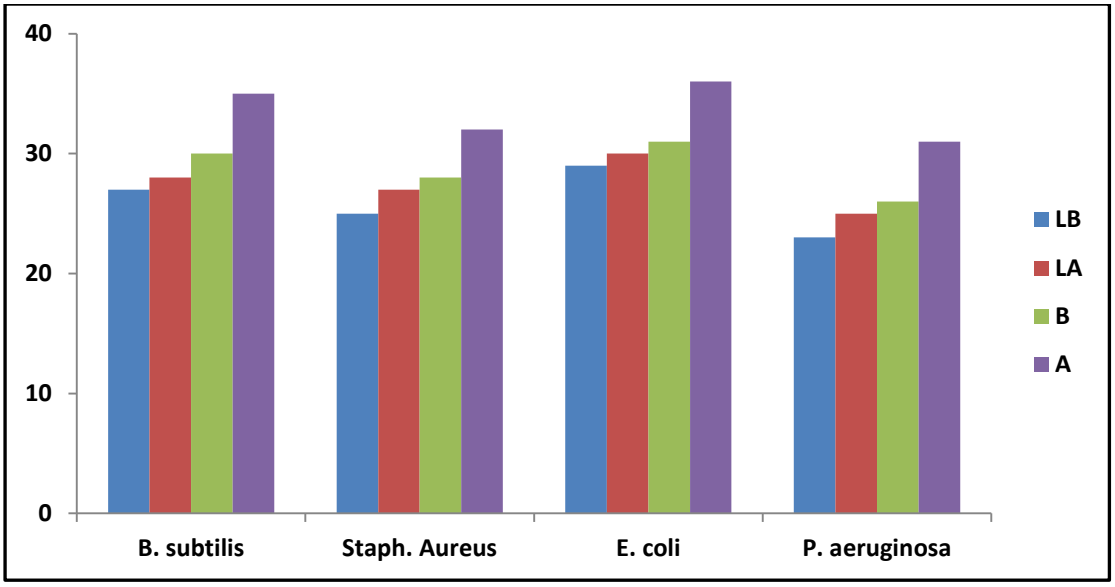

Figure 4: the antibacterial activity of Zn(II) complex and ligand before (LB,B) and after (LA, A) irradiation at a concentration of 10 mg ml $^{-1}$ in relation to gentamycin and ampicillin as standard medications

3.6. Cytotoxicity

Applying the MTT test assay, the compounds' in vitro cytotoxicity against the human MCF7 breast cancer cell line was assessed. Mitochondrial dehydrogenase activity, a measure of cell viability, is quantified using the MTT assay. IC_{50} values were determined via non-linear regression for the ligand and Zn^{2+} complex against MCF7 cells at various concentrations (31.25–1000 µg/mL) (Abdalla et al., 2020; Al-Farhan et al., 2021; Alshater et al., 2023). Cytotoxicity results (Table S2, Figure 5) showed that, compared to cisplatin, activity followed the order: cisplatin > A > B > LA > LB.

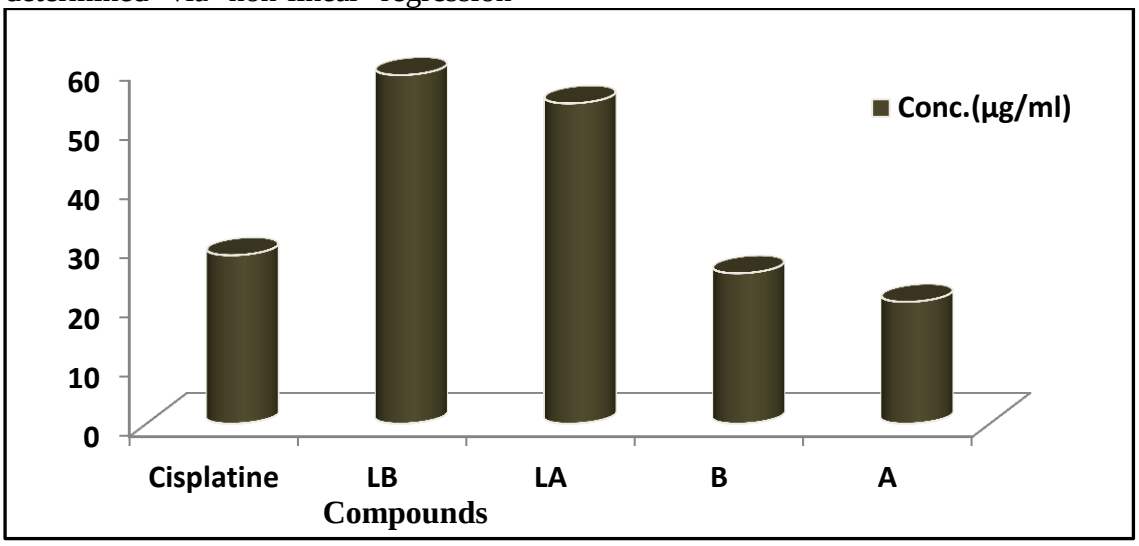

Figure 5. IC_{50} values of Zn (II) complex and ligand against MCF7 cancer cell line in comparison to cisplatin before (LB, B) and after (LA, A) irradiation.

4. CONCLUSION

The Zn(II) complex was synthesized and characterized using spectroscopic and structural techniques. Based on thermal analysis, FTIR, molar conductivity, and elemental data, the complex was assigned a 1:1 M:L stoichiometry with the formula [$ZnLCl_2$]. Its biological activity was evaluated against various bacterial strains and the MCF7 cell line, revealing enhanced efficacy after irradiation.

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