SYNTHESIS, CHARACTERIZATION, ANTI-MICROBIAL AND CYTOTOXIC APPLICATIONS OF ZINC(II) COMPLEXES

Muhammad Tariq, Atia Batool, Naseem Abbas, Ajaz Hussain, Ahmad Kaleem Qureshi and Jafir Hussain Shirazi

1Institute of Chemical Sciences, Bahauddin Zakariya University, 60800-Multan, Pakistan
2Department of Chemistry, University of Sahiwal, Sahiwal 57000, Pakistan
3Department of Pharmacy, The Islamia University of Bahawalpur 63100, Pakistan

(Received September 14, 2020; Revised April 29, 2021; Accepted May 6, 2021)

ABSTRACT. In the present research, three zinc(II) complexes were synthesized using 3-(3-fluorophenyl)-2-methylacrylic acid (HL), 1,10-phenanthroline and 2,2'-pyridine as ligands. The composition, structural confirmation, coordination way of ligand and assignment of geometry to the complexes were made by different analytical tools like elemental analysis, FTIR and 'H-NMR. The ligand 3-(3-fluorophenyl)-2-methylacrylate appeared to coordinate the metal (Zn) atom via COO moiety in all of the complexes (1-3) while 1,10-phenanthroline and 2,2'-pyridine coordinated to Zn(II) atom through N-donor sites in complexes 2 and 3, respectively. The complex 1 showed four while 2 and 3 showed six co-ordinated geometry. The synthesized complexes were evaluated for antimicrobial and cytotoxic activities. The obtained results showed that complexes are active against microbial agents and exhibited significant cytotoxicity.

KEY WORDS: Co-coordination, Geometry, Zinc(II) complexes, Biological activity

INTRODUCTION

Zn(II) as cation has a very promising ability to catalyse many biochemical reactions [1]. Zn plays an inhibitory role in the growth of bacterial strains like E. coli, S. faecalis, etc [2]. This may be attributed to Zn(II) cation interaction with cell membrane protein resulting in its deactivation and disturbance in transport of nutrients [3]. Interaction of Zn(II) with O-donor ligand and N-donor ligand bring a valuable change in the biological activities [4]. N-donor ligands having heterocyclic rings like 1,10-phenanthroline, 2,2'-pyridine enhance anti-microbial activities [5-8].

Zinc(II) carboxylates have been studied extensively for the last three decades due to their bioactive role in anti-microbial activities [9-11]. Carboxylic acids have very important role to enhance lipophilic character and biochemical processes in metabolic pathways [12]. Substituted carboxylic acids are more promising in enhancing bioactive role of metal and have rich mode of co-ordination with metal centre [13-16]. Various modes of co-ordination like monodentate, bidentate leading to tetrahedral and octahedral geometry have been reported [17, 18].

The research work on metal carboxylate complexes is a growing area to explore some novel anti-bacterial, anti-fungal and cytotoxic compounds in order to cope resistance problems. With this continuation and growing research field, we have synthesized three complexes of Zn(II) with both carboxylic acid and N-donor ligands and found out their anti-microbial and cytotoxic activities.

EXPERIMENTAL

Chemicals and methods

The analytical rank chemicals, methylmalonic acid (99%), 3-fluorobenzaldehyde (99%), zinc chloride, 1,10-phenanthroline, 2,2'-pyridine and piperidine (99.5%) were bought from an

*Corresponding author. E-mail: mtnazir@yahoo.com
This work is licensed under the Creative Commons Attribution 4.0 International License
international chemical supplier company Sigma-Aldrich and utilized as received without further purification. The organic solvents were bought from Merck (Germany). The solvents were dried by applying typical procedures [19]. Gallenkamp electrothermal melting point apparatus made in UK was used to find out melting point of ligand and synthesized compounds. Thermo Nicolet-6700 FT-IR instrument was utilized to have FT-IR spectra in the range of 4000-400 cm\(^{-1}\). \(^1\)H NMR spectra were recorded by 300 MHz NMR spectrometer made up of Bruker (Switzerland).

### Syntheses

The 3-(3-fluorophenyl)-2-methylacrylic acid (HL) was prepared using 3-fluorobenzaldehyde (14 mmol, 1.736 g), methylmalonic acid (28 mmol, 3.305 g) and piperidine (28 mmol, 2.38 g) taken in 1:2:2 molar ratio (Scheme 1). The reactant mixture was refluxed in double neck flask using pyridine as solvent for 24 h at 100 °C. After refluxing, the reactant mixture was cooled at room temperature and then put into ice water with addition of concentrated HCl. The solution pH was maintained at 3. The solid product was obtained by filtration which was then washed with water and dried in air.

\[
\begin{align*}
\text{F} & \quad \text{H} \\
\text{C} & \quad \text{H} \\
\text{C} & \quad \text{O} \\
\text{H} & \quad \text{C} \\
\text{C} & \quad \text{C} \\
\text{O} & \quad \text{H} \\
\text{H} & \quad \text{COOH} \\
\text{H} & \quad \text{COOH} \\
\text{H} & \quad \text{C} \\
& \quad \text{F}
\end{align*}
\]

**Scheme 1**

The stoichiometric amount of aqueous solution of NaHCO\(_3\) was added drop by drop to methanolic solution of ligand acid (HL) and reaction mixture was put on stirring for 2 h at 25 °C (Scheme 2). The resultant mixture was rotary evaporated to get required product.

\[
\begin{align*}
\text{F} & \quad \text{H} \\
\text{C} & \quad \text{H} \\
\text{C} & \quad \text{O} \\
\text{H} & \quad \text{C} \\
\text{C} & \quad \text{C} \\
\text{O} & \quad \text{H} \\
\text{H} & \quad \text{COOH} \\
\text{H} & \quad \text{COOH} \\
\text{H} & \quad \text{C} \\
& \quad \text{F}
\end{align*}
\]

**Scheme 2**

The complex 1 was synthesized by reacting zinc chloride (0.136 g, 1.0 mmol) and NaL (0.404 g), in 1:2 molar ratio (Scheme 3) in dry methanol. The reaction mixture was kept on stirring for 5 h at 25 °C. The insoluble NaCl was detached via filtration. The filtrate was evaporated to get the final product.

\[
\begin{align*}
2\text{Na} & \quad + \quad \text{ZnCl}_2 \\
a) \text{methanol} & \quad \text{b) 25 °C} \\
\text{L}_2\text{Zn} & \quad + \quad 2\text{NaCl}
\end{align*}
\]

**Scheme 3**

*Bull. Chem. Soc. Ethiop. 2021, 35(2)*
Synthesis, characterization, anti-microbial and cytotoxic applications of zinc(II) complexes

The complex 2 was synthesized by the reacting the mixture of zinc(II) chloride (0.136 g, 1.0 mmol), sodium salt of ligand (0.404 g, 2.0 mmol) and 1,10-phenanthroline (0.18 g, 1.0 mmol) in dry methanol (Scheme 4) at 25 °C for 5 h. The insoluble NaCl was detached by filtration. The filtrate was evaporated to get final product.

Step 1.

\[ 2\text{LNa} + \text{ZnCl}_2 \xrightarrow{\text{methanol}} \text{L}_2\text{Zn} + 2\text{NaCl} \]

Step 2.

\[ \text{L}_2\text{Zn} + \text{L}' \xrightarrow{\text{methanol}} \text{L}_2\text{ZnL}' \]

\[ \text{L}' = 1,10\text{-phenanthroline} \]

Scheme 4

The complex 3 was synthesized by the reacting the mixture of zinc(II) chloride (0.136 g, 1.0 mmol), sodium salt of ligand (0.404 g, 2.0 mmol) and 2,2'-pyridine (0.156 g, 1.0 mmol) (Scheme 5) in dry methanol at 25 °C for 5 h. The insoluble NaCl was detached via filtration and product was acquired by evaporating the solvent through rota-vapour.

Step 1.

\[ 2\text{LNa} + \text{ZnCl}_2 \xrightarrow{\text{methanol}} \text{L}_2\text{Zn} + 2\text{NaCl} \]

Step 2.

\[ \text{L}_2\text{Zn} + \text{L}'' \xrightarrow{\text{methanol}} \text{L}_2\text{ZnL}'' \]

\[ \text{L}'' = 2,2'\text{-bipyridine} \]

Scheme 5

RESULTS AND DISCUSSION

The ligand 3-(3-fluorophenyl)-2-methylacrylic acid (HL) was synthesized successfully using procedure given in experimental section. The results along with characterization data are represented as: Yield: 1.96 g, 78.0%. melting point 142-145 °C. Elemental analysis for C_{10}H_{14}FO_{2} calculated (%): C, 66.66, H 5.03. Found (%): C, 66.01, H 4.92. Infrared (KBr, cm\(^{-1}\)): 3417.8 \(\nu\)(OH), 1634.3 \(\nu\)(OCO)\(_{asym}\), 1392.1 \(\nu\)(OCO)\(_{sym}\) (\(\Delta\nu = 242.2\) cm\(^{-1}\)). Proton-NMR (DMSO ppm): 12.53 (s, H1, 1H), 6.85 (s, H3, 1H), 7.209-8.735 (m, ArH, 4H), 1.67 (s, H10, 3H). The

Bull. Chem. Soc. Ethiop. 2021, 35(2)
complexes ZnL₂ (1), ZnL₃Phen (2) and ZnL₂bipy (3) were synthesized successfully using procedure given in experimental section.

**Complex 1**

Yield: 0.29 g, 69.0%. m.p. 160-162 °C. Chemical formula: C₉H₆F₃O₂Zn, formula mass: 424 g/mol. Elemental analysis: calculated (%): C, 56.69, H 3.81. Found (%): C, 56.12, H 3.96. Infrared (KBr, cm⁻¹): 1560 ν(OCO)ₘₛₘ, 1402 ν(OCO)ₘₚₘ (Δν = 158 cm⁻¹), 441 ν(Zn-O). ¹H-NMR (DMSO, ppm): 6.44 (s, H₃, 1H), 7.03-7.38 (m, ArH, 4H), 1.67 (s, H₁₀, 3H).

**Complex 2**

Yield: 0.48 g, 79.0%. m.p. 110-112 °C. Chemical formula: C₁₂H₁₁F₂N₂O₂Zn, formula mass: 604 g/mol. Elemental analysis: calculated (%): C, 63.64, H 4.01. Found (%): C, 63.05, H 4.12. Infrared (KBr, cm⁻¹): 1537.8 ν(OCO)ₘₚₘ, 1393.8 ν(OCO)ₘₛₘ (Δν = 144 cm⁻¹), 441 ν(Zn-O), 452 ν(Zn-N). ¹H-NMR (DMSO, ppm): 6.46 (s, H₃, 1H), 7.10-7.89 (m, ArH, 4H), 1.74 (s, H₁₀, 3H), 8.09-9.08 (m, Phen H).

**Complex 3**

Yield: 0.45 g, 79.0 %. m.p. 120-122 °C. Chemical formula: C₁₃H₁₂F₂N₂O₂Zn, formula mass: 580 g/mol. Elemental analysis: calculated (%): C, 62.13, H 4.17. Found (%): C, 61.95, H 4.01. Infrared (KBr, cm⁻¹): 1518.4 ν(OCO)ₘₚₘ, 1396.4 ν(OCO)ₘₛₘ (Δν = 122 cm⁻¹), 427 ν(Zn-O), 486 ν(Zn-N). ¹H-NMR (DMSO, ppm): 6.60 (s, H₃, 1H), 7.30-7.75 (m, ArH, 8H), 1.76 (s, H₁₀, 6H), 8.03-8.38 (m, Phen H).

**Fourier transform-infrared spectroscopy**

The newly prepared ligand and complexes were characterized firstly by FT-IR Spectrophotometer (Nicolet-6700 FT-IR) in the array of 4000-400 cm⁻¹. The FT-IR spectra of ligand and complexes (1-3) are represented in Figures 1-4. The characteristic values of vibrational frequencies of complexes were correlated with their precursors to confirm syntheses of complexes [20]. The decrease in Δν value in complexes in comparison to higher Δν values in ligand (HL) support the formation of complexes, the νₘₚₘ(COO⁻) frequencies move to lesser while νₘₛₘ(COO⁻) to higher frequency [21, 22]. The divergence of asymmetric and symmetric frequencies of COO⁻ moiety (Δν) indicates the co-ordinating way of COO⁻ moiety with Zn atom. If the value of Δν difference is larger than 200 cm⁻¹, it represents a monodentate co-ordination while Δν value smaller than 200 cm⁻¹ indicates bidentate co-ordinating way of COO⁻ moiety with metal atom [23, 24]. In present study, the Δν in Zn(II) complexes have been observed as 158 (1), 122 (2) and 146 (3), showing chelated nature of co-ordination. The disappearance broad band of ν(OH) and emergence of a new Zn-O vibration band in region 400–450 cm⁻¹ indicate the binding of O- atom with Zn metal in complexes. While emergence of a Zn-N vibration band at 486 (2) and 452 cm⁻¹ (3) shows coordination of nitrogen with zinc atom.

**Proton-nuclear magnetic resonance studies**

Proton-NMR of ligand and its zinc(II) complexes (1-3) were recorded using Bruker 300 MHz NMR and the representative spectra are represented in Figures 5-6. DMSO was used as a solvent. The ¹H-NMR interpretation has been done by using the names and numbering in precursors as given in Scheme 6. The pattern of intensity and peak multiplicity are used to allot.

*Bull. Chem. Soc. Ethiop. 2021, 35(2)*
Synthesis, characterization, anti-microbial and cytotoxic applications of zinc(II) complexes

**Figure 1.** FT-IR spectrum of 3-(3-fluorophenyl)-2-methylacrylic acid (HL).

**Figure 2.** FT-IR spectrum of complex 1.

Bull. Chem. Soc. Ethiop. **2021**, 35(2)
Figure 3. FT-IR spectrum of complex 2.

Figure 4. FT-IR spectrum of complex 3.
the values to proton resonance signals [25, 26]. The formation of zinc complexes was confirmed by the disappearance of acidic proton peak at 12.36 ppm. The olefinic proton (R\(^1\)CH=CR\(^2\) (R\(^2\) COOH)) appeared at 6.85, 6.44, 6.46 and 6.60 ppm in ligand HL, complexes 1, 2 and 3, respectively. While aromatic protons and heterocyclic organic rings protons appeared at their expected values.

Figure 5. Proton-NMR spectrum of 3-(3-flourophenyl)-2-methylacrylic acid (HL).

Figure 6. Proton-NMR spectrum of Zn(II)PhenL\(_2\).
The proposed structures of complexes ZnL₂ (1), ZnL₂Phen (2) and ZnL₂bipy (3) are represented in Figure 7.
Synthesis, characterization, anti-microbial and cytotoxic applications of zinc(II) complexes

Figure 7. Proposed structures of complexes ZnL₂ (1), ZnL₂Phen (2) and ZnL₂bipy (3).

Anti-microbial and cytotoxic investigations

Ligand and the Zn(II) complexes (1-3) were subjected for In vitro anti-bacterial potential evaluation. Four bacterial strains named as Bordetella bronchi septica, Escherichia coli, Micrococcus luteus and Staphylococcus aureus were used in the experiment using Agar well-diffusion process [27]. Two anti-biotic drugs Cefixime and Roxithromycin were taken as +ve control while DMSO as a solvent and negative control. The outcomes are represented in Table 1. Anti-bacterial activity was evaluated by measuring zone of inhibition in millimetre (mm). There are three main parameters, significant (> 20 mm), better (< 20 mm) and insignificant (< 10 mm) to explain the results [28]. The results showed that zinc(II) complexes (1-3) are comparatively more active than ligand HL but comparable or less than reference drugs used. The microbe’s killing was may be due to enzyme retardation, impairment in cell membrane or Tweedy’s Chelation Theory [29]. The chelates (metal complexes) decrease the polarity and increase lipophilicity of metal complexes which help in crossing the cell membrane made up of lipid layer [30].

Table 1. Antibacterial activity data of ligand and its Zn(II) complexes (1-3).

| Ligand/complex | Staphylococcus aureus | Escherichia coli | Bordetella bronchiseptica | Micrococcus luteus |
|----------------|-----------------------|------------------|--------------------------|-------------------|
| HL             | 0                     | 10               | 06                       | 10                |
| 1              | 10                    | 10               | 12                       | 0                 |
| 2              | 12                    | 22               | 25                       | 20                |
| 3              | 16                    | 18               | 10                       | 16                |
| Cefixime       | 23                    | 23               | 26                       | 21                |
| Roxithromycin  | 26                    | 21               | 26                       | 23                |

Concentration: 1 mg mL⁻¹ of DMSO. Reference drugs, Roxithromycin and Cefixime 1 mg mL⁻¹.

The newly prepared ligand and its zinc(II) complexes (1-3) were tested against four fungal strains named as Aspergillus flavus, Fusarium solani, Aspergillus fumigates and Aspergillus niger. This activity was determined using Agar Tube Dilution method [31] and the results in the form of % inhibition are represented in Table 2. Terbinafine was taken as +ve control. The
criteria to explain results is % growth inhibition in four slabs, > 70, 70–60, 60–50 and < 50% growth inhibition measured as significant, good, moderate and non-significant, respectively [28]. The results revealed that zinc(II) complexes (1-3) are more active than ligand acid (HL). The complex 3 showed highest antifungal activity among the complexes. The nitrogen containing ligand enhance antifungal activity that may be due to higher permeation ability into cell. This is attributed to proper overlapping of metal ion and nitrogen donor ligand orbital which results partial sharing of positive charge on metal ion with ligand orbital. Thus reduction of polarity on metal ion lead to more lipophilic character of metal complex, allowing it to cross lipid membrane of fungus and show more potent activity [32-34].

Table 2. Antifungal activity data of ligand and its Zn(II) complexes (1-3).

| Ligand/complex | Aspergillus flavus | Aspergillus niger | Aspergillus fumigatus | Fusarium solani |
|----------------|-------------------|------------------|----------------------|----------------|
| HL             | 40                | 20               | 30                   | 10             |
| 1              | 25                | 75               | 50                   | 40             |
| 2              | 80                | 55               | 70                   | 60             |
| 3              | 100               | 65               | 70                   | 80             |
| Terbinafine    | 99                | 99               | 99                   | 99             |

*In vitro* method of agar tube dilution, concentration: 200 µg mL⁻¹ DMSO.

**In vitro cytotoxic assessment**

The cytotoxic studies of ligand and Zn(II) complexes (1-3) were evaluated via brine-shrimp lethality procedure [31] and standard drug was MS-222 (*Tricaine Methane sulfonate*). The results are shown in Table 3. The results exhibited that generally, the tested Zn(II) complexes have shown more cytotoxicity than ligand but less than their reference drug used.

Table 3. Cytotoxicity data of ligand and its Zn(II) complexes (1-3).

| Ligand/complex | No. of shrimp killed out of 20 per dilution* |
|----------------|--------------------------------------------|
|                | 1000 µg/mL | 100 µg/mL | 10 µg/mL |
| HL             | 15         | 12        | 05       |
| 1              | 14         | 11        | 10       |
| 2              | 20         | 16        | 18       |
| 3              | 20         | 18        | 15       |
| Vehicle control| 0          | 0         | 0        |

*Against* brine-shrimp (*in vitro*). The standard drug was MS-222 (*Tricaine Methane sulfonate*).

**CONCLUSION**

Three new Zn(II) complexes using O and N-donor mixed ligands were prepared and characterized by elemental analysis, FT-IR, ¹H and ¹³C NMR spectroscopic methods. The FT-IR studies showed that carboxylate ligand co-ordinate with Zn(II) ion in bidentate fashion. The complex 1 exhibited four co-ordinated while complexes 2 and 3 six co-ordination behaviour around metal atom. The antimicrobial results showed that Zn(II) complexes 1-3 exhibit good antimicrobial activity than the ligand. The cytotoxic studies revealed that complexes 2 and 3 were more toxic than complex 1 and ligand (HL).
Synthesis, characterization, anti-microbial and cytotoxic applications of zinc(II) complexes

ACKNOWLEDGEMENT

The authors are thankful to Bahauddin Zakariya University Multan, Pakistan for financial support during the research work.

REFERENCES

1. Kargar, H.; Behjatmanes, R.; Torabi, V.; Kashani, M.; Chavoshpour, Z.; Kazemi, Z.; Mirkhani, V.; Sahraei, A.; Tahir, M.N.; Ashfaq, M.; Munawar, K.S. Synthesis, characterization, crystal structures, DFT, TD-DFT, molecular docking and DNA binding studies of novel copper(II) and zinc(II) complexes bearing halogenated bidentate N,O-donor Schiff base ligands. *Polyhedron* 2020, 23, 114988.

2. Hijazi, A.A.; Mohanad, D.; Darawsheh, Emilia, R. Synthesis, crystal structure, spectroscopic and biological properties of mixed ligand complexes of zinc(II) valproate with 1,10-phenanthroline and 2-aminomethylpyridine. *Polyhedron* 2013, 61, 235-241.

3. Maret, W. Zinc biochemistry: From a single zinc enzyme to a key element of life. *Adv. Nutr. Res.* 2013, 4, 82-91.

4. Mohammad, A.S.; Mohammad, W.; Mohammad, J.A.; Agata, T.K.; Rafal, K.; Mahboob, A.; Saud, I.R.; Sourabh, D.; Mohammad, R.K.; Mohammad, S.; Nader, T. Synthesis, structural investigations and pharmacological properties of a new zinc complex with a N4-donor Schiff base incorporating 2-pyridyl ring. *Inorg. Chim. Acta* 2019, 487, 97-106.

5. Uddin, N.; Sirajuddin, M.; Uddin, N.; Wazir, H.; Tariq, M.; Tirmzi, S.A. Synthesis, spectroscopic characterization, biological screenings, DNA binding study and POM analyses of transition metal carboxylates. *Spectrochim. Acta A Mol. Biomol. Spectros.* 2015, 140, 563-574.

6. Kargar, H.; Amir, A.A.; Muhammad, N.T.; Muhammad, A.; Khurram, S.M. Synthesis, spectral characterization, crystal structure determination and antimicrobial activity of Ni(II), Cu(II) and Zn(II) complexes with the Schiff base ligand derived from 3,5-dibromosalicylaldehyde. *J. Mol. Struct.* 2021, 1229, 129842.

7. Abdur, R.; Afzal, S.; Khurram, S.M.; Saqib, Ali.; Mohammad, N.T.; Mohsin, J.; Asad, M.K. Synthesis, physicochemical elucidation, biological screening and molecular docking studies of a Schiff base and its metal(II) complexes. *Arab. J. Chem.* 2020, 13, 1130-1141.

8. Nairita, H.; Sagar, G.; Sasanka, S.M. Synthesis, crystal structure and spectroscopic properties of a new type of pentanuclear zinc(II) complex. *Inorg. Chim. Acta* 2019, 491, 34-41.

9. Hafeez, S.T.; Saqib, Ali.; Muhammad, N.T.; Muhammad, Iqbal.; Khurram, S.M. One-pot synthesis, structural elucidation, DNA binding and alkaline phosphatase inhibition studies of zinc(II) complexes with 4-nitrocinamic acid and ethylenediamine. *J. Coord. Chem.* 2014, 67, 2479-2495.

10. Niaz, M.; Muhammad, I.; Abdul, W.; Sadia, R.; Shaukat, S.; Erum, Mehreen, G.; Shahnaz, R.; Muzzamil, Shah.; Carola, S. Synthesis, crystal structure, DNA binding and molecular docking studies of zinc(II) carboxylates, *Spectrochim. Acta A Mol. Biomol. Spectros.* 2018, 190, 368-377.

11. Dipankar, D.; Subhadip, R.; Dutta, R.N.; Raghavaiah, P.; Patrick, M. Zinc carboxylates containing diimine: Synthesis, characterization, crystal structure, and luminescence. *J. Mol. Struct.* 2013, 1053, 127-133.

12. Nasima, A.; Naeem, A.; Moazzam, H.B.; Naghma, R.; Muhammad, N.T.; Samreen, S.; Bushra, M. Synthesis, crystal structure, DNA binding and in vitro biological studies of Ni(II), Cu(II) and Zn(II) complexes of N-phthaloylglycine. *J. Photochem. Photobiol. B: Biology* 2012, 117, 228-239.
13. Wang, F.Q.; Weng, D.F.; Zheng, X.J.; Zang, J.J.; Mad, H.; Jin, L.P. 3D supramolecular network assembly and thermal decomposition of new copper(II) complexes with pyrazine-2,6-dicarboxylic acid. Inorg. Chem. Acta 2007, 360, 2029-2038.

14. Tariq, M.; Ali, S.; Muhammad, N.; Sirajuddin, M.; Shah, N.A.; Tahir, M.N.; Khalid, N. Synthesis, spectroscopic characterization, X-ray structures, biological screenings, DNA interaction study and catalytic activity of organotin(IV) 3-(4-Fluorophenyl)-2-methylacrylic acid derivatives. J. Organomet. Chem. 2013, 723, 79-89.

15. Sirajuddin, M.; McKee, V.; Tariq, M.; Ali, S. Newly designed organotin(IV) carboxylates with peptide linkage: Synthesis, structural elucidation, physicochemical characterizations and pharmacological investigations. Eur. J. Med. Chem. 2018, 143, 1903-1918.

16. Tariq, M.; Sirajuddin, M.; Ali, S.; Khalid, N.; Tahir, M.N. Pharmacological investigation and Petra/Osiris/Molinspiration(POM) analyses of newly synthesized potentially bioactive organotin(IV) carboxylates derivatives. Russ. J. Gen. Chem. 2017, 87, 2690-2698.

17. Tariq, M.; Sirajuddin, M.; Ali, S.; Khalid, N.; Shah, N.A. Biological evaluations and spectroscopic characterizations of 3-(4-ethoxyphenyl)-2-methylacrylate based organotin(IV) carboxylates derivatives. J. Photochem. Photobio. B 2016, 158, 174-183.

18. Tariq, M.; Sirajuddin, M.; Ali, S.; Muhammad, N.; Shah, N.A.; Sirajuddin, M.; Tahir, M.N.; Khalid, N. Biological screening, DNA interaction studies and catalytic activity of organotin(IV) 2-(4-ethylbenzylidene) butanoic acid derivatives: Synthesis, spectroscopic characterization and X-ray structure. J. Coord. Chem. 2014, 67, 323-340.

19. Perrin, D.D.; Armarego, W.L.F. Purification of Laboratory Chemicals, 3rd ed., Pergamon Press: Oxford, 2003.

20. Danish, M.; Ali, S.; Badshah, A.; Mazhar, M.; Masood, H.; Malik, A.; Kehr, G. 1H, 13C, 119Sn NMR, 119Sn Mössbauer, infrared and mass spectrometric studies of organotin carboxylates of 2-(2,3-dimethylphenyl) aminobenzoic acid and their effect on microorganisms. Synth. React. Inorg. Met.-Org. Chem. 1997, 27, 863-885.

21. Xie, Q.; Yang, Z.; Jiang, L. Preparation, structure and biological activities of mixed methylcyclohexyltin carboxylates. Main Group Met. Chem. 1996, 19, 509-520.

22. Choi, K.Y. 2D Hydrogen-bonded polymer assembled by zinc(II) tetraaza macrocyclic complex and 1,2-cyclopentanedicarboxylic acid. Main Group Met. Chem. 2014, 37, 125-129.

23. Fang, X.; Song, X.; Xie, Q. Synthesis and structural characterization of several tris (2-methyl-2-phenylpropyl) tin carboxylates containing germanium. J. Organomet. Chem. 2001, 619, 43-48.

24. Eng, G.; Song, X.; Zapata, A.; de Dios, A.C.; Casabianca, L.; Pike, R.D. Synthesis, structural and larvicidal studies of some triorganotin 2-(p-chlorophenyl)-3-methylbutyrates. J. Organomet. Chem. 2007, 692, 1398-1404.

25. Bhatti, M.H.; Ali, S.; Masood, H.; Mazhar, M.; Qureshi, S.I. Synthesis, spectroscopic characterization and biological studies of organotin derivatives of 2-(2,6-dichlorophenyl) aminophenyl acetic acid. Synth. React. Inorg. Met.-Org. Chem. 2000, 30, 1715-1729.

26. Ali, S.; Ahmad, F.; Mazhar, M.; Munir, A.; Masood, M.T. Synthesis and spectral studies of di- and triorganotin(IV) complexes with 2-(6-methoxynaphthyl) propionic acid (naproxen). Synth. React. Inorg. Met.-Org. Chem. 2001, 32, 357-372.

27. Zhang, Y.; Wang, X.; Ding, L. Synthesis and DNA binding studies of Mg(II) complex of Schiff base derived from vanillin and L-tryptophan. Nucleos. Nucleot. Nucl. 2011, 30, 49-62.

28. Rehman, A.; Choudhary, M.I.; Thomsen, W.J. Bioassay Techniques for Drug Development, Harwood Academic Publishers: Amsterdam, 2001.

29. Sirajuddin, M.; Ali, S.; Haider, A.; Shah, N.A.; Shah A.; Khan M.R. Synthesis, characterization, biological screenings and interaction with calf thymus DNA as well as electrochemical studies of adducts formed by azomethine [2-(3,5-dimethylphenylimino) methyl] phenol and organotin(IV) chlorides. Polyhedron 2012, 40, 19-31.
Synthesis, characterization, anti-microbial and cytotoxic applications of zinc(II) complexes

30. Tweedy, B.G. Plant extracts with metal ions as potential antimicrobial agents. *Phytopathology* **1964**, *55*, 910-914.

31. John, R.P.; Sreekanth, A.; Rajakannan, V.; Ajith, T.A.; Kurup, M.R.P. New copper(II) complexes of 2-hydroxyacetophenone N(4)-substituted thiosemicarbazones and polypyridyl co-ligands: Structural, electrochemical and antimicrobial studies. *Polyhedron* **2004**, *2*, 2549-2559.

32. Mayer, B.N.; Ferrigni, N.R.; Putnam, J.E.; Jacobson, L.B.; Nichols, D.E.; Mclaughlin J.L. Brine shrimp: A convenient general bioassay for active plant constituents. *Planta Med.* **1982**, *45*, 31-34.

33. Sara, N.S.; Fabio, Z. Recent studies on the antimicrobial activity of transition metal complexes of groups 6–12. *Chemistry* **2020**, *2*, 418-452.

34. Agwara, M.O.; Ndifon P.T.; Ndosiri, N.B.; Paboudam, A.G.; Yufanyi, D.M.; Mohamadou, A. Synthesis, characterisation and antimicrobial activities of cobalt(II), copper(II) and zinc(II) mixed-ligand complexes containing 1,10-phenanthroline and 2,2′-bipyridine. *Bull. Chem. Soc. Ethiop.* **2010**, *24*, 383-389.