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EXPLORING THE BIOLOGICAL ACTIVITY OF ORGANOTIN CARBOXYLATE COMPLEXES WITH 4-SULFOSALICYLIC ACID

Dhekra Jawad Hashim[1], Enass J. Waheed[2], Angham G. Hadi[3*] and Sadiq J. Baqir[4]

[1]Technical Institute of Babylon, Al-Furat Al-Awsat Technical University, Babylon, Iraq
[2]Department of Chemistry, College of Education for Pure Sciences, Ibn-Al-Haitham, University of Baghdad, Baghdad, Iraq
[3]Chemistry Department, College of Science, Babylon University, Babylon, Iraq
[4]Medical Laboratories Techniques Department, Al-Mustaqbal University College, Babylon Iraq

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ABSTRACT. 4-Sulfosalicylic acid (SSA) was used as a ligand to prepare new triphenyltin and dimethyl-tin complexes by condensation with the corresponding organotin chloride salts. The complexes were identified by different techniques, such as infrared spectra (tin and proton), magnetic resonance, and elemental analyses. The ^{119}Sn-NMR was studied to determine the prepared complexes' geometrical shape. Two methods examined the antioxidant activity of (SSA) and prepared complexes; Free radical scavenging activity (DPPH) and CUPRRAC methods. Tri and di-tin complexes gave high percentage inhibition than ligands with both methods due to tin moiety; the triphenyltin carboxylate complex was the best compared with the others. Also, antibacterial activity was assessed by using the agar ditch method against **(***Escherichia coli*) and (*Staphylococcus aureus*) bacteria. The complexes gave high activity in inhibition than the ligand derived. Also Triphenyltin carboxylate complex showed higher antibacterial activity than the dimethyltin complex against two types of bacteria **(***Escherichia coli) and (Staphylococcus aureus).*

KEY WORDS: Antioxidant activity, Antibacterial activity, Sulfosalicylic acid, Tri phenyl tin chloride, *Escherichia coli*, *Staphylococcus aureus* bacteria

INTRODUCTION

Organotin(IV) complexes' synthetic chemistry became more active. The subject of study is motivated by widespread industrial and antimicrobial applications. These compounds have been used as biocides, catalysts, and potent polymer heat stabilizers. Many processes, including polyurethane structure, esterification, antifouling coatings, silicone curing, inter-esterification of vegetable oil to biodiesel, and PVC stabilizers, can benefit from the employment of organotin carboxylates as catalysts [1-10]. They can also be used for several types of synthesis. Antibacterial and antifungal medical chemicals are advantageous medications.

Medications can harm malignancies by binding to DNA phosphor di esterase [11-14]. Its organotin(IV) moieties and related ligands may be typically linked to its antibacterial activity. Triorganotin compounds are known to have higher activity than binary or mono tin-organic analogs because of their ability to bind to proteins [14-18]. They have, furthermore, offered excellent anti-tumor and anti-cancer responses.

Among other things, the major characteristic is a mineral component, which boosts the biological activity of organotin(IV) complexes and makes them more effective antioxidants than a pure organic binder. Antioxidants can slow or stop organisms from oxidizing when exposed to oxygen from the environment or atmosphere. They stabilize food, cosmetics, petrochemicals, and polymer compounds. Antioxidants are a component of the body's defensive system against medicines [19-21].

*Corresponding author. E-mail: sci.angam.ganem@uobabylon.edu.iq

This study seeks to investigate the antioxidant and antimicrobial activity of the Sn(IV) complex and determine whether there is an improvement or decline in antioxidant activity when compared to both the 4-Sulfosalicylic acid and the organotin(IV) complexes formed from it.

EXPERIMENTAL

Synthesis of Ph_3SnCl complex

The molar ratio (metal:ligand) to synthesize the complex was 1:1, since an appropriate amount of Ph3SnCl (1.9273 g, 5 mmol) was dissolved in 20 mL of hot methanol then added to the stirred solution of (SSA) (1.7369 g, 5.0 mmol) that dissolved in 30 mL of methanol with 5 mmol of NaOH, the mixture was stirred at room temperature for 10 min then refluxed for 4 hours. The resulting solution was filtered, washed, dried, and recrystallized to form precipitation [22].

Synthesis of Me_2SnCl_2 complex

The molar ratio (metal:ligand) to synthesize the complexes is 1:2 since Me_2SnCl_2 (0.8787 g, 4.0 mmol) was dissolved in 20 mL of methanol and then added to the stirred solution of (SSA) (2.7791 g, 8 mmol, in 30 mL methanol) with 8 mmol NaOH. This mixture was refluxed for 4 hours. The resulting solution was filtered, dried, and recrystallized to form precipitation [23].

Antioxidant activity tests

a) DPPH technique. Antioxidant activity was measured using the 1,1-diphenyl-2-picrylhydrazine (DPPH) technique, as described by others [24, 25]. The compounds were dissolved in methanol at different concentrations of 2; 4; 8; 16, and 32 M, respectively. DPPH (0.1 mM in methanol) was added to each test solution and carefully mixed. After 30 minutes, the solution was discarded. A UV-Vis spectrophotometer was used to test the mixture's absorbance at a wavelength of 517 nm. The proportion of inhibition against DPPH was used to calculate antioxidant activity. The percentage inhibition was calculated using equation (1);

$$I\% = \left[\frac{Cotrol\ Absorbance - Sample\ Absorbance}{Control\ Absorbance}\right] \times 100 \quad (1)$$

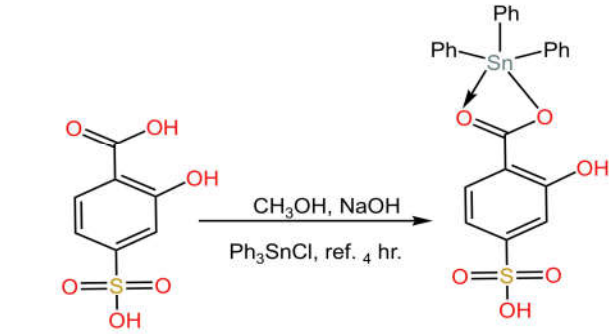
b) CUPRAC method. Antioxidant activity test by CUPRAC method was performed according to method used by others [26].

$$Total\ antioidants\ levals\ = \left[\frac{A\ test}{A\ STD}\right] \times Conce.of\ STD\ \left(\frac{mmole}{L}\right) \quad (2)$$

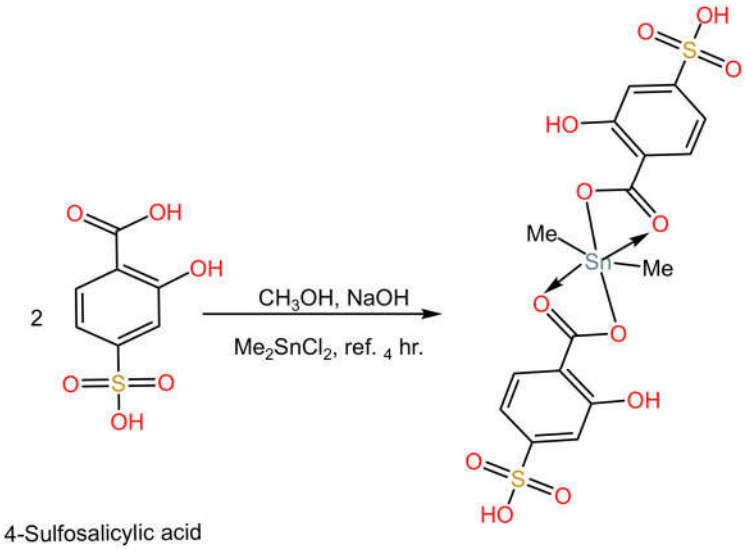
RESULTS AND DISCUSSION

*Synthesis of organotin(IV) complexes **1** and **2***

The new complexes were obtained by refluxing methanolic solutions of tri and di-organotin chloride with (SSA), respectively, with a high yield percentage, as shown in Schemes 1 and 2).



Scheme 1. Complex **1** preparation.



Scheme 2. Complex **2** preparation.

4-sulfosalicylic acid (SSA) and its complexes were identified using FTIR, proton and ^{119}Sn-NMR spectroscopy techniques, as well as elemental analyses. Tables 1-3 summarize the findings of each study.

Table 1. Physical analysis data of (SSA) and its complexes.

Compound	Color	Yield %	MP (°C)	Elemental analysis % calculated (found)		
				C	H	S
(SSA)	Yellowish white	-	119-121	38.54(39.24)	2.77(2.98)	14.69(14.27)
Ph_3SnL	Grey	91.7	225-227	52.94(53.91)	3.55(4.21)	5.65(5.43)
Me_2SnL_2	Off white	94.3	197-199	32.96(33.64)	2.77(3.45)	11.00(11.76)

The elemental analysis of compounds gave good agreement between calculated and found values, with high yield percentage.

The infrared spectrum data for (SSA) characterize a strong band at 1676 cm^{-1} associated with the C=O stretch and a broad band 2400-3350 cm^{-1} related to the carboxyl group, since these groups have been shifted and gone due to complexation. New bands appeared at 513-443cm^{-1} related to Sn-C and Sn-O bonds, respectively.

Table 2. IR spectral data of (SSA) and its complexes.

Compound	C-O	C=O	Sn-C	Sn-O
(SSA)	1608	1676	-	-
Ph-4-sulfosalicylic acid	1598	1678	513	443
Me-4-sulfosalicylic acid	1612	1672	516	449

^{1}H-NMR Spectra of (SSA) show three different signals at 15.46, 11.5 and 8.5 ppm related to OH–groups of (alcohol, carboxylic acid and sulfuric acid) respectively. The benzene ring at 7.26-7.5 ppm. All these signals were shifted due to complexation as in Table 3. The ^{119}Sn-NMR was studied to find out the geometrical shape of the prepared complexes, with a value less than 200 indicating five coordination complexes and a value greater than 200 indicating six coordination complexes with an octahedral shape [27], Accordingly, the complex is of six coordination and octahedral shape.

Table 3. ^{1}H-NMR Spectra of (SSA) and complexes.

Compound	^{1}H-NMR	^{119}Sn-NMR
(SSA)	15.46 (s, 1H, alcohol gr.), 11.5(s, 1H, COOH gr.), 8.5 (s, 1H, SO_3H gr.), 7.26-7.5 (m, 5H, Aromatic H),	---
Ph-4- sulfosalicylic acid	15.34 (s, 1H, alcohol gr.), 8.5 (s, 1H, SO_3H gr.), 7.52-8.33 (m, 5H, Aromatic H), 7.30-7.49 (m, 5H, phenyl gr),	-179
Me-4- sulfosalicylic acid	15.42 (s, 1H, alcohol gr.), 8.5 (s, 1H, SO_3H gr.), 7.57-8.35 (m, 5H, Aromatic H), 0.71-0.92 (s, 6H, 2Me)	-224

Biological activity

The two synthesized complexes were examined in varied quantities using the two procedures outlined in the antioxidant activity analysis. After obtaining the absorbance in each measurement, the percent inhibition was computed; also, the results are displayed in Figures 1 and 2.

As shown in Figures 1 and 2 In both methods, the oxidation activity of the prepared complexes was higher than that of the ligand from which they were derived, as well as the oxidation activity of the triple phenyl complex was higher than that of the dimethyl complex, and this is due to the presence of the three phenyl groups in addition to the increase in aromatization

Also, the antibacterial activity of substances was assessed in vitro using the agar ditch method against *S. aureus* and *E. coli* [28]. The stock solutions were made by dissolving (40 mg) each component in 1 mL of ethanol, from which two-fold serial dilutions were obtained. The inhibition diameter of the ligand and its complexes with three different concentrations (25%, 50%, and 100%) for (24 h) has been shown in (25%, 50 h) has been shown in Table 4 and Figure 3 [29].

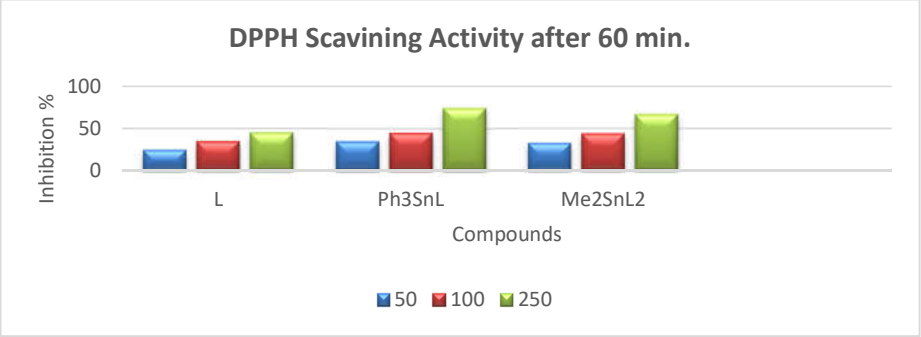


Figure 1. DPPH scavenging activity of (SSA) and its complexes.

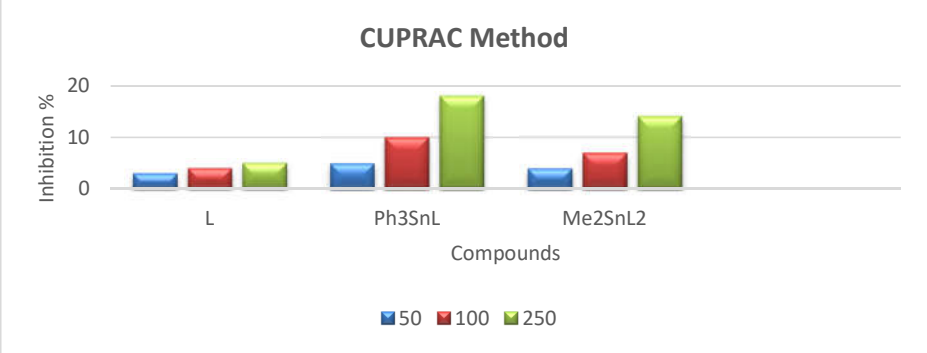


Figure 2. CUPRAC Method activity of (SSA) and its complexes

Table 4. Zone of inhibition of antibacterial action.

No.	Compound	*E. coli(-)*			*S. aureus(+)*		
		25%	50%	100%	25%	50%	100%
1	(SSA)	11	12	15	6	6	8
2	Ph-4- sulfosalicylic acid	48	56	60	25	31	38
3	Me-4- sulfosalicylic acid	35	37	40	17	19	24

The ligand shows low antibacterial activity compared to their complexes. The coordination of the ligand with the metal improved its activity. Many literature reports indicate that inactive or less active become more active with coordination or complexation [30-33]. Chelation and coordination, following the overtones concept, reduce the polarity of the metal ion primarily due to the partial sharing of its positive charge with donor groups throughout the entire chelate ring system. The central metal atom's lipophilic nature is thus increased through the chelation process, which favors its permeation through the lipoid layer of the membrane and makes it easier for the metal complex to cross the bacterial membrane, increasing the activity of complexes [34-37]. Triphenyltin carboxylate complex gave higher antibacterial activity than dimethyl-tin complex, against two types of bacteria (*Escherichia coli*) and (*Staphylococcus aureus*), this may be related to the presence of three phenyl groups and higher aromaticity.

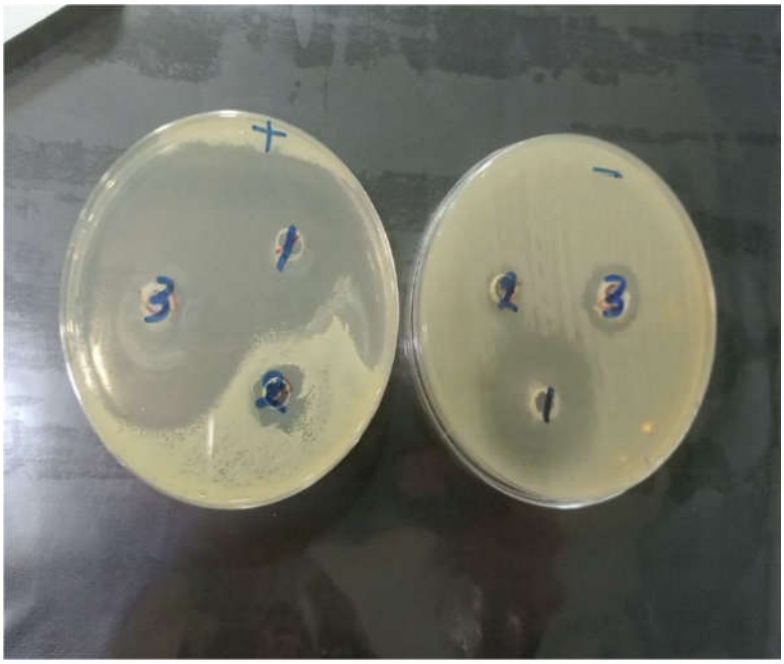


Figure 3. Zone of inhibition of antibacterial action.

CONCLUSION

In conclusion, this work has shown that new organic tin complexes can be prepared with a high yield ratio by condensing sulfosalicylic acid with triphenyltin or dimethyl tin salts. These complexes were identified using various methods and have the potential to be used as both antioxidants and antibacterial agents. What's most impressive is that the prepared complexes exhibited significantly higher biological activity compared to the ligands used in the synthesis process.

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REFERENCES

1. Ghani, H.; Yousif, E. Chemistry of some organotin compounds. *Al-Nahrain J. Sci*. **2021**, 24, 9-15.
2. Pascual, J.; Flatken, M.; Félix, R.; Li, G.; Turren-Cruz, S.H.; Aldamasy, M.H; Abate, A. Inside back cover: Fluoride chemistry in tin halide Perovskites (Angew. Chem. Int. Ed. 39/2021). *Angew. Chem. Int. Ed*. **2021**, 60, 21595-21595.
3. Hussain, S.; Ali, S.; Shahzadi, S.; Tahir, M.N.; Shahid, M. Synthesis, characterization, biological activities, crystal structure and DNA binding of organotin(IV) 5-chlorosalicylates. *J. Coord. Chem.* **2015**, 68, 2369-2387.

4. Schuchardt, U.; Sercheli, R.; Vargas, R.M. Transesterification of vegetable oils: A review. *J. Braz. Chem. Soc.* **1998**, 9, 199-210.
5. Yousif, E.; Salih, N.; Salimon, J. Improvement of the photostabilization of PVC films in the presence of 2N-salicylidene-5-(substituted)-1,3,4-thiadiazole. *J. Appl. Polym. Sci.* **2011**, 120, 2207-2214.
6. Yousif, E.; Salimon, J.; Salih, N. Improvement of the photostabilization of PVC films in the presence of thioacetic acid benzothiazole complexes. *Malaysain J. Agric. Sci*. **2011**, 15, 81-92.
7. Omae, I. Organotin antifouling paints and their alternatives. *Appl. Organomet. Chem.* **2003**, 17, 81-105.
8. Katsoulakou, E.; Tiliakos, M.; Papaefstathiou, G.; Terzis, A.; Raptopoulou, C.; Geromichalos, G.; Manessi-Zoupa, E. Diorganotin(IV) complexes of dipeptides containing the α-aminoisobutyryl residue (Aib): Preparation, structural characterization, antibacterial and antiproliferative activities of [(n-Bu) 2Sn (H−1L)](LH = H-Aib-L-Leu-OH, H-Aib-L-Ala-OH). *J. Inorg. Biochem.* **2008**, 102, 1397-1405.
9. Arraq, R.R.; Hadi, A.G.; Ahmed, D.S.; El-Hiti, G.A.; Kariuki, B.M.; Husain, A.A.; Yousif, E. Enhancement of photostabilization of poly (vinyl chloride) in the presence of tin–cephalexin complexes. *Polym.* **2023**, 15, 550.
10. Hadi, A.G.; Yousif, E.; El-Hiti, G.A.; Ahmed, D.S.; Jawad, K.; Alotaibi, M.H.; Hashim, H. Long-term effect of ultraviolet irradiation on poly (vinyl chloride) films containing naproxen diorganotin(IV) complexes. *Molecules* **2019**, 24, 2396.
11. Schwartsmann, G.; Ratain, M.J.; Cragg, G.M.; Wong, J.E.; Saijo, N.; Parkinson, D.R.; Di Leone, L. Anticancer drug discovery and development throughout the world. *J. Clin Oncol.* **2002**, 20, 47S-59S.
12. Neidle, S.; Thurston, D.E. Chemical approaches to the discovery and development of cancer therapies. *Nat. Rev. Cancer.* **2005**, 5, 285-296.
13. Khan, M.I.; Baloch, M.K.; Ashfaq, M. Biological aspects of new organotin(IV) 14. Compounds of 3-maleimidopropionic acid. *J. Organomet Chem.* **2004**, 689, 3370-3378.
14. Al-Rikabi, E.H.; Al-Refai, R.A.; Baqir, S.J.; Hadi, A.G.; Al-Qayyim, A.K. Synthesis, structure, and in vitro cytotoxic activity of two organotin complexes of 2-[(2, 3-dimethylphenyl) amino] benzoic acid. *J. Med. Chem. Sci.* **2023**, 6, 1230-1238.
15. Kang, W.; Wu, X.; Huang, J. Synthesis, crystal structure and biological activities of four novel tetranuclear di-organotin (IV) carboxylates. *J. Organomet. Chem.* **2009**, 694, 2402-2408
16. Tabassum, S.; Pettinari, C. Chemical and biotechnological developments in organotin cancer chemotherapy. *J. Organomet. Chem.* **2006**, 691, 1761-1766.
17. Höti, N.; Ma, J.; Tabassum, S.; Wang, Y.; Wu, M. Triphenyl tin benzimidazolethiol, a novel antitumor agent, induces mitochondrial-mediated apoptosis in human cervical cancer cells via suppression of HPV-18 encoded E6. *J. Biochem.* **2003**, 134, 521-528.
18. Gielen, M.; Biesemans, M.; De Vos, D.;Willem, R. Synthesis, characterization and in vitro antitumor activity of di-and triorganotin derivatives of polyoxa-and biologically relevant carboxylic acids. *J. Inorg. Biochem.* **2000**, 79, 139-145.
19. Bukhari, S.B.; Memon, S.; Mahroof-Tahir, M.; Bhanger, M.I. Synthesis, characterization and antioxidant activity copper–quercetin complex. *Spectrochim. Acta Part A: Mol. Biomol. Spectrosc.* **2009**, 71 5 1901-1906.
20. Pisoschi, A.M.; Negulescu, G.P. Methods for total antioxidant activity determination: A review. *Biochem. Anal. Biochem.* **2011**, 11, 106.
21. Litescu, S.C.; Eremia, S.A.; Diaconu, M.; Tache, A.; Radu, G.L. Biosensors publications on assessment of reactive oxygen species and antioxidants. *Environ. Biosens*. **2011**, 95-114, DOI: 10.5772/16250.
22. Arraq, R.R.; Hadi, A.G. Enhanced the antioxidant activity of triorganotin(IV) complexes derived from cephalexin. *Azerb. Med. J.* **2022**, 62, 6.

23. Arraq, R.R.; Hadi, A.G. Synthesis, identification, and anti-oxidant activity of di-organotin (IV)-cephalexin complexes. *J. Med. Chem. Sci.* **2023,** 6, 392-401.
24. Marinova, G.; Batchvarov, V. Evaluation of the methods for determination of the free radical scavenging activity by DPPH. *Bulg. J. Agric. Sci.* **2011**, 171 11-24.
25. Kontogiorgis, C.; Hadjipavlou-Litina D. Biological evaluation of several coumarin derivatives designed as possible anti-inflammatory/antioxidant agents *J. E. Inhibit. Med. Chem.* **2003***,* 181 63-69.
26. Apak, R.; Güçlü, K.; Demirata, B.; Özyürek, M.; Celik, S.; Bektaşoğlu, B.; Berker, KL.; Özyurt D. Comparative evaluation of various total antioxidant capacity assays applied to phenolic compounds with the CUPRAC assay. *Molecules* **2007**, 12 7 1496-547.
27. Rehman, W.; Baloch, M.K.; Badshah, A; Ali, S. Synthesis and characterization of biologically potent di-organotin (IV) complexes of mono-methyl glutarate. *J. Chin. Chem. Soc.* **2005**, 522 231-236.
28. Rehder, D. Biological and medicinal aspects of vanadium. *Inorg. Chem. Commun*. **2003**, 6, 604-617.
29. Drevenšek, P.; Zupančič, T.; Pihlar, B.; Jerala, R.; Kolitsch, U.; Plaper, A.; Turel, I. Mixed-valence Cu(II)/Cu(I) complex of quinolone ciprofloxacin isolated by a hydrothermal reaction in the presence of L-histidine: Comparison of biological activities of various copper–ciprofloxacin compounds. *J. Inorg. Biochem.* **2005**, 99, 432-442.
30. Kulkarni, A.D.; Patil, S.A.; Naik, V.H; Badami, P.S. DNA cleavage and antimicrobial investigation of Co(II), Ni(II), and Cu(II) complexes with triazole Schiff base: Synthesis and spectral characterization. *Med. Chem. Res*. **2011**, 20, 346-354.
31. Nejo, A.A.; Kolawole, G.A.; Nejo, A.O. Synthesis, characterization, antibacterial, and thermal studies of unsymmetrical Schiff base complexes of cobalt(II). *J. Coord. Chem*. **2010**, 63, 4398-4410.
32. Elgamasy, S.M.; Abd-ElRazek, S.E. Binuclear transition metal complexes containing 6N moieties Schiff base ligand: Synthesis, characterization and microbicide activities. *Bull. Chem. Soc. Ethiopia*. **2023**, 37, 901-915.
33. Aftab, M.; Mazhar, N.; Shah, M.T.; Batool, M.A.M.; Mahmud, T.; Basra, M.A.R.; Bratu, G.; Mitu, L. Synthesis, characterization and biological evaluation of three new Schiff bases derived from amino acids and their Ag(I) complexes. *Bull. Chem. Soc. Ethiopia*. **2022**, 36, 45-56.
34. Chohan, Z.H.; Munawar, A.; Supuran, C.T. Transition metal ion complexes of Schiff bases: Synthesis, characterization and antibacterial properties. *Met. Based Drugs* **2001**, 8, 137-143.
35. Chohan, Z.H.; Iqbal, M.S.; Aftab, S.K. Design, synthesis, characterisation and antibacterial properties of copper(II) complexes with chromone derived compounds. *Appl. Organomet. Chem*. **2010**, 24, 47-56.
36. Coombs, R.R.; Westcott, S.A.; Decken, A.; Baerlocher, F.J. Palladium(II) Schiff base complexes derived from sulfanilamides and aminobenzothiazoles. *Transit. Met. Chem*. **2005**, 30, 411-418.
37. Apak, R.; Güçlü, K.; Demirata, B.; Özyürek, M.; Celik, S.; Bektaşoğlu, B.; Berker, K.L.; Özyurt, D. Comparative evaluation of various total antioxidant capacity assays applied to phenolic compounds with the CUPRAC assay *Molecules* **2007**, 12, 1496-1547.