

Cobalt and Iron-based Heteroleptic Complexes of Imidazole: Synthesis, Antibacterial and Hemolytic Potential

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ABSTRACT

Transition metal complexes can deliver exciting properties in the development of metal-based drug system. The aim of current study is to synthesis of metal complexes and to evaluate their biological properties such as antibacterial and hemolytic activity to know their biological importance. Five cobalt and iron-based complexes (1-5), [Co^{II}(imiH)(benz)(N₃)] (1), [Fe^{II}(imiH)(piv)(N₃)] (2), [Fe^{II}(imiH)(benz)(N₃)] (3), [Fe^{II}(imiH)(N₃)₂] (4), [Fe^{II}(imiH)(piv)₂] (5), (where imiH = imidazole, piv = pivalic acid, N₃⁻ = azide, benz = benzoic acid) were produced by the reacting of respective metal salts with selective ligands. These complexes were characterized through FTIR and elemental analyses. Compounds (1-5) were tested for their antibacterial biofilm inhibition and hemolytic studies. Complexes of 3 (85.42%) and 2 (69.58%) have promising inhibition for *S. aureus* whereas 5 (70.48%) and 2 (62.94%) also exhibit significant inhibition against *E. coli*. The hemolytic study of these metal complexes indicates the cytotoxicity against bovine erythrocytes. The current study will be useful for the development metallodrugs in future.

Keywords: Transition metal complexes, Carboxylates, Imidazole, Sodium azide, Biological studies.

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INTRODUCTION

Metal-based complexes are the fascinating class of research to diagnose the diseases and to work as a therapy against them.¹⁻³ Some metal complexes were employed for the cure of various diseases like Wilson's, Alzheimer's, cancer and some of these were also utilized to control the development of other pathogens and parasites.⁴ Therefore, it is important to synthesize those novel therapeutic and diagnostic agents which exhibit low side effects and can be used for human diseases.^{5,6} Regardless of the tremendous work in the metal-based drug development field still we are way far off to successfully utilize a compound for various diseases.⁷ The coordination chemistry of

imidazole containing compounds displays significant medicinal and biological uses.⁸ Imidazole contains various natural products such as histidine, nucleic acid, purine and histamine. Besides, it is a polar and ionizable compound which is used as a remedy.⁹ Transition metal ions complexes containing imidazole have particular interest due to their relationship with biological systems.¹⁰ Controlling infectious diseases is still a remarkable problem due to the increase of multi-drug resistant microbial pathogens. Also, conventional treatment is usually not able to control resistant microorganisms and consequently the probability of death.¹¹



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Therefore, a quest to find a metal-based drug system should be in process.

Carboxylate ligands possess characteristics like (i) carboxylate groups have diversity in coordination modes; (ii) carboxylates can rotate in some extent that may connect in different directions with metal ions.¹² On the other hand, azide is also a unique ligand and can act as a variety of co-ordination modes such as monodentate and a bridging ligand.^{13,14}

Out of various biological activities, cytotoxicity tests are important to understand the mechanisms of action of chemicals on cells and tissues. Cytotoxicity of compounds has significant value in different pathological processes, carcinogenesis and inflammation.¹⁵

In previous, imidazole also has been explored to synthesize transition metal ions-based complexes which are used for different biological studies such as antibacterial, antifungal and DNA-binding.¹⁶

Owing to the need of metal complexes in medicine and biological research area, we also have been contributed and reported cobalt complex with bio-film inhibition, hemolytic and anti-thrombolytic studies,¹⁷ Co (II), Ni (II), Cu (II) and Zn (II) coordination compounds with urease inhibitory activities¹⁸ and some Mn(II), Cu(II) complexes with antioxidant activity and docking studies.¹⁹ Recently, we also explored the Ni(II) complex along with antimicrobial and DFT properties.²⁰ To continue work in this field of research, at that time, we selected Co and Fe metal ions with mixed ligands approach. Therefore, herein, along with imidazole, we also employ carboxylates and sodium azide to construct Co and Fe based metal complexes and are screened for biofilm inhibition and hemolytic studies.

EXPERIMENTAL

MATERIALS AND METHODS

All the reagents were purchased from Sigma Aldrich Company and these were used as such and solvents were distilled. FTIR spectra were measured on Thermo scientific USA model Nicolet 6700 and PREVISAGE-21 Shimadzu Spectrophotometer Japan respectively through KBr pellets in the 4000- 400 cm^{-1} range. Elemental analysis was performed on a Vario Micro Cube, Elementar.

Synthesis of complexes: (1-5)

Synthesis of $[\text{Co}^{\text{II}}(\text{imiH})(\text{benz})(\text{N}_3)]$ (1)

$\text{CoCl}_2 \cdot 2\text{H}_2\text{O}$ (0.08 g, 0.5 mmol) was added in MeOH (10 ml) with constant stirring until dissolved and imidazole (0.04 g, 0.5 mmol), benzoic acid (0.12 g, 1 mmol) and

NaN_3 (2 mmol, 0.13 g) were added in MeOH (10 ml) respectively. The resulting solution was further stirred and within 2-3 days, m gained the product, washed with MeOH and dried in air.

Synthesis of $[\text{Fe}^{\text{II}}(\text{imiH})(\text{piv})(\text{N}_3)]$ (2)

A solution of $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (0.1 g, 0.5 mmol), sodium azide (0.07 g, 1mmol) and pivalic acid (0.10 g, 1 mmol) in MeOH (10 ml) was inserted to a solution of imidazole (0.03 g, 0.5 mmol) in MeOH (10 ml) with constant stirring. The solution was filtered and the filtrate was left for crystallization and after one-week product was obtained, washed with MeOH solvent, dried in air and collected.

Synthesis of $[\text{Fe}^{\text{II}}(\text{imiH})(\text{benz})(\text{N}_3)]$ (3)

A solution of imidazole (0.03 g, 0.5 mmol), in MeCN (10 ml) was introduced to a stirred solution of $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ (0.14g, 0.5 mmol), benzoic acid (0.12 g, 1mmol) and sodium azide (0.07 g, 0.5 mmol) in MeOH (10 ml). The resulting solution was further stirred and after 3 days product was obtained, washed and dried.

Synthesis of $[\text{Fe}^{\text{II}}(\text{imiH})(\text{N}_3)_2]$ (4)

In a solution of imidazole (0.03 g, 0.5 mmol) in MeOH (10 ml), pivalic acid (0.051 g, 0.5 mmol) and sodium azide (0.07 g, 0.5 mmol) was added with continuous stirring. The mixture was further stirred and finally $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (0.1 g, 0.5 mmol) in MeCN (10 ml) was added under continuous stirring. The obtained mixture was filtered and left undisturbed. After two days, the material was collected, washed with CH_3CN and dry out in air.

Synthesis of $[\text{Fe}^{\text{II}}(\text{imiH})(\text{piv})_2]$ (5)

$\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ (0.2 g, 1 mmol) pivalic acid (0.20 g, 2mmol) and sodium azide (0.03g, 0.5 mmol) were dissolved in MeCN (20 ml). In stirred solution, imidazole (0.07 g, 1mmol) was introduced added under stirring then resulting mixture was left for slow evaporation and within a three days product was collected and dried in air.

Protocol for Antibacterial biofilm inhibition assay

All the synthesized coordination compounds (1-5) were tested *in vitro* for antibacterial study against Gram-negative *E. coli* and Gram-positive *S. aureus* bacterial strains using biofilm assay.

Microtiter Plate method was employed to study the formation of bacterial biofilm.²¹ The entire experiments were performed in triplicate for chosen bacterial strains. The % age of bacterial growth inhibition were calculated as follows:

$$\text{Inhibition (\%)} = 100 - (\text{OD}_{630 \text{ sample}} \times 100) / \text{OD}_{630 \text{ control}}$$

Protocol for Hemolytic activity

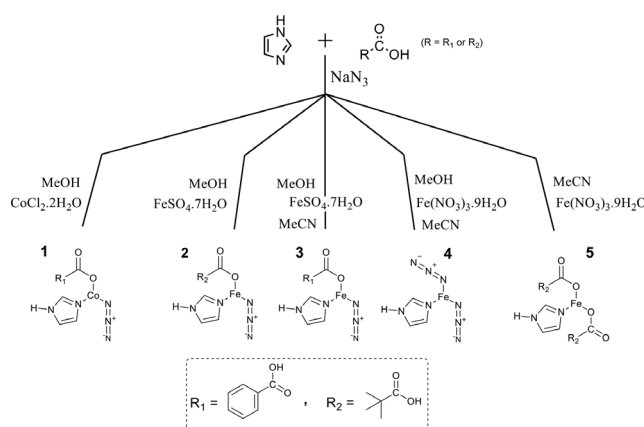
Hemolytic activity for 1-5 were studied according to the already presented procedure.²² In this protocol, bovine erythrocytes were collected from Department of Clinical Medicine and Surgery, University of Agriculture, Faisalabad, Pakistan. In sterile isotonic phosphate-buffered saline solution (PBS), red blood cells were maintained and, in this method, erythrocytes with $\sim 10^8$ cells mL^{-1} were employed. In this method, negative control was phosphate buffer saline and positive control employed was Triton X-100. In this assay, the absorbance at 576 nm was assessed through microplate reader (BioTeK, USA) and the hemolysis % age of each compound was determined.

RESULTS AND DISCUSSION

Complexes (1-5) were synthesized by using cobalt and iron metal salts with imidazole, carboxylates and sodium azide. The synthesis is illustrated in Scheme 1. The obtained materials were characterized by FTIR with range $4000\text{--}400\text{ cm}^{-1}$ and elemental analysis (Table 1). They were further evaluated for bacterial biofilm inhibition and hemolytic studies.

FTIR Studies

A carboxylate ligand may connect to the metal in various modes including monodentate or bidentate



Scheme 1: Synthesis of mixed ligand complexes 1 to 5.

and as a result relative positions of the asymmetric and symmetric stretching vibrations are obtained. The strong intensity bands of $\nu_{\text{sym}}(\text{COO})$ and $\nu_{\text{asym}}(\text{COO})$ stretching vibrations of the coordinated carboxylate anion were observed in the range $1632\text{--}1322\text{ cm}^{-1}$, respectively. The large separation between the stretching vibrations [i.e., $\Delta\nu = \nu_{\text{asym}}(\text{COO}) - \nu_{\text{sym}}(\text{COO}) \sim 250$] signifies an unsymmetrical monodentate mode of bonding of the carboxylate group.

The carboxylate bridging in the compound was detected due to display of medium intensity band at $\sim 945\text{ cm}^{-1}$ in the molecule. The $\nu(\text{C}=\text{N})$ and $\nu(\text{C}=\text{C})$ stretching vibration peaks appeared in the region $1580\text{--}1430\text{ cm}^{-1}$. A strong band accredited to the presence of νCH of the aromatic ring appears at 2965 cm^{-1} for 1, 2939 cm^{-1} for 2, 2958 cm^{-1} for 3, 2957 cm^{-1} for 4 and 2961 cm^{-1} for 5 respectively. The IR absorption band at 3312 cm^{-1} , 3237 cm^{-1} , 3277 cm^{-1} , 3308 cm^{-1} , 3221 cm^{-1} are given to the stretching vibrations of the N-H groups for the complexes 1-5. The imidazole ring was proved by the stretching vibrations of C=C and C=N bonds at 1585 cm^{-1} and 1489 cm^{-1} (1), 1587 and 1414 cm^{-1} (2), 1585 and 1410 cm^{-1} (3), 1578 and 1493 cm^{-1} (4) 1589 and 1485 cm^{-1} (5) respectively. Also, the absorption peaks at $768, 708, 704, 766, 765\text{ cm}^{-1}$ can be ascribed to the out of plane bending of C-H bonds in complexes 1-5 respectively. Previously, imidazole-based co-ordination compounds with Co, Cu and Zn were reported and their absorption has been found in above-mentioned ranges.²³

The complexes 1-4 exhibited strong bands in $2062, 2066, 2060, 2064\text{ cm}^{-1}$ which were attributed to the co-ordination of N_3^- ions as a terminal ligand with a metal ion. According to this fact, the primary oxidation states of the metal ions Co(II), Fe(II) were satisfied by the presence of N_3^- ions inside the coordination sphere.

Biological studies

The results of the biological evaluation such as bacterial biofilm inhibition and hemolytic activity for complexes

Table 1: Detail of complexes (1-5).

Complexes	Molecular Formula	Colour	Formula Weight (g/mol)	% age yield	Elemental Analysis, calculated (Found)		
					C	H	N
1.	$\text{CoC}_{10}\text{H}_9\text{O}_2\text{N}_5$	Pink	290.15	42	41.30 (41.02)	3.13 (2.95)	24.14 (24.16)
2.	$\text{FeC}_8\text{O}_2\text{H}_{15}\text{N}_5$	Reddish brown	267.07	55	35.98 (35.73)	4.91 (4.68)	26.22 (26.15)
3.	$\text{FeC}_{10}\text{H}_9\text{O}_2\text{N}_5$	Yellow	287.05	39	41.84 (41.23)	3.16 (3.24)	24.40 (24.05)
4.	$\text{FeC}_3\text{H}_4\text{N}_8$	Brick red	207.97	57	17.33 (1.95)	1.94 (1.82)	53.88 (3.47)
5.	$\text{FeC}_{13}\text{H}_{22}\text{O}_4\text{N}_2$	Reddish brown	326.17	36	47.87 (47.79)	6.80 (6.42)	8.59 (8.27)

(1-5) are summarized in Table 2. The obtained results are also depicted graphically in Figures, 1-3.

All the complexes were checked against *E. coli* and *S. aureus* bacterial species relative to standard drug, Rifampicin. The order of decreasing efficacy is $5 > 2 > 1 > 3 > 4$ and $3 > 2 > 1 > 4 > 5$ for *E. coli* and *S. aureus*, respectively. The complexes 5 and 4 exhibited promising biofilm inhibition activity; 70.48% and 62.94% respectively against *E. coli*. Similarly, complex 3, 2 and 1 showed significant activity like 85.42%, 69.58% and 51.04% against *S. aureus*. It has been noted earlier that different factors like chelate effects and sort of the ligands, entire charge, nuclearity, presence of counter-ions and nature of ligands may affect antimicrobial inhibition.

Ligands donor sites such as N- and O- are also important to prevent the formation of enzyme and those enzymes that need these groups for activity are much susceptible to deactivation through metal ions chelation.²⁴

Mainly, the polarity of the metal ion is lowered by chelation as a result of sharing of its partial positive charge with the donor atoms and the π - electron delocalization

Table 2: Bacterial biofilm inhibition and hemolytic activities of complexes (1-5).

Compounds	Biofilm inhibition assay (%)		% age Hemolysis
	<i>E. coli</i>	<i>S. aureus</i>	
1	2.43	51.04	10.98
2	62.94	69.58	9.33
3	-	85.42	11.65
4	-	-	10.32
5	70.48	-	-
Rifampicin	81.4	86.8	-
Phosphate Buffer	-	-	0.00
TritonX-100	-	-	100

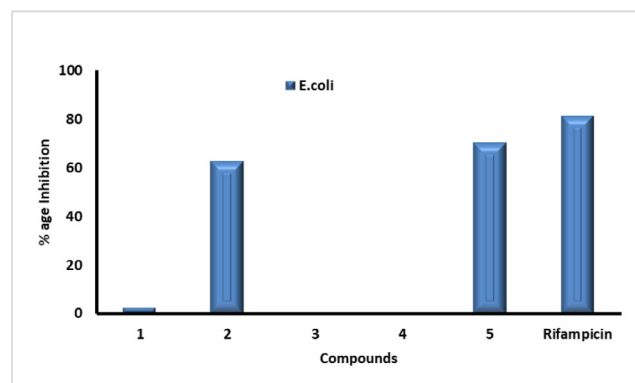


Figure 1: Antibacterial biofilm inhibition against *E. coli* for complexes (1-5).

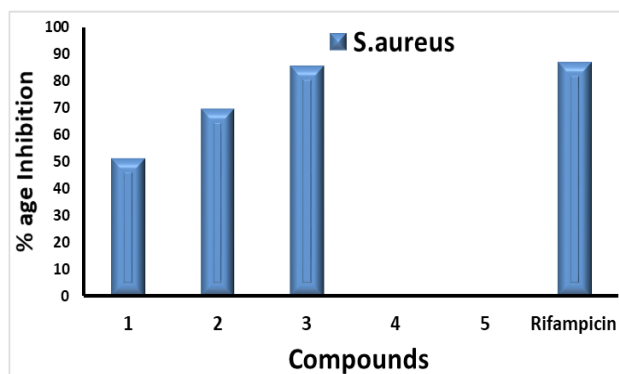


Figure 2: Antibacterial biofilm inhibition for *S. aureus* of complexes (1-5).

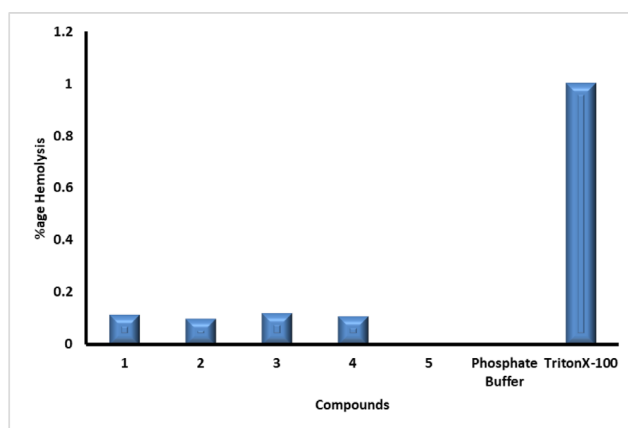


Figure 3: Hemolytic activity of heteroleptic complexes (1-5).

that occurs in a chelate ring upon coordination.²⁵ Due to chelation, the lipophilic nature of the central metal atom is increased that makes it feasible for passing over the lipid layer of the bacterial cell membrane²⁶ and useful to increase liposolubility of the molecule and hydrophobic nature. In this way, the biological exploitation ratio and task of the test compounds is increased.²⁷

The hemolytic studies of complexes (1-5) were tested to check the cytotoxicity by means of negative control and the positive controls such as PBS and Triton-X-100 as references. The obtained results demonstrate that all the complexes have hemolytic activity against bovine erythrocytes.

CONCLUSION

Complexes (1-5) were prepared by the reaction of respective metal salts with imidazole and carboxylates (pivalates/benzoates) in the presence of sodium azide along with MeOH / MeCN respectively. All the metal complexes were screened for bacterial biofilm inhibition and hemolytic activities. Bacterial biofilm

inhibition study indicated that complexes 3 (85.42%) and 2 (69.58%) showed promising inhibition against *S. aureus* while compounds 5 (70.48%) and 2 (62.94%) also displayed notable activity against *E. coli*. Furthermore, the hemolytic study revealed that all compounds were found to be slightly toxic. The present work will be useful for future study in medicinal inorganic chemistry research area.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

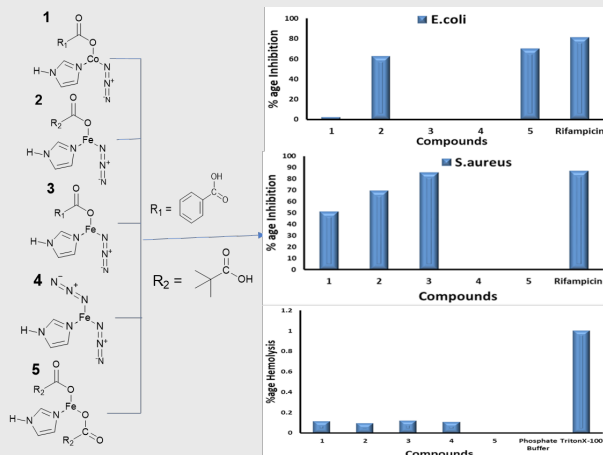
ABBREVIATIONS

imiH: Imidazole; **piv**: Pivalic acid; **N³⁻**: azide; **benz**: Benzoic acid; **FTIR**: Fourier Transform Infrared Spectroscopy; **MeOH**: Methanol; **MeCN**: Acetonitrile.

REFERENCES

- Mjos KD, Orvig C. Metallo drugs in medicinal inorganic chemistry. *Chem Rev*. 2014;114(8):4540-63. doi: 10.1021/cr400460s, PMID 24456146.
- Sodhi RK. Metal Complexes in Medicine: An Overview and Update from Drug Design Perspective. *CTOIJ*;14(2). doi: 10.19080/CTOIJ.2019.14.555883.
- De Almeida A, Bonsignore R. Fluorescent metal-based complexes as cancer probes. *Bioorg Med Chem Lett*. 2020;30(13):127219. doi: 10.1016/j.bmcl.2020.127219, PMID 32360103.
- Iranshahy M, Javadi B. Diet therapy for the treatment of Alzheimer's disease in view of traditional Persian medicine: a review. *Iran J Basic Med Sci*. 2019;22(10):1102-17. doi: 10.22038/ijbms.2019.36505.8694, PMID 31998450.
- Franz KJ, Metzler-Nolte N. Introduction: metals in medicine. *Chem Rev*. 2019;119(2):727-9. doi: 10.1021/acs.chemrev.8b00685, PMID 30990707.
- Ndagi U, Mhlongo N, Soliman ME. Metal complexes in cancer therapy – an update from drug design perspective. *Drug Des Dev Ther*. 2017;11:599-616. doi: 10.2147/DDDT.S119488, PMID 28424538.
- Leon IE, Cadavid-Vargas JF, Di Virgilio ALD, Etcheverry SB. Vanadium, ruthenium and copper compounds: a new class of nonplatinum metallo drugs with anticancer activity. *Curr Med Chem*. 2017;24(2):112-48. doi: 10.2174/0929867323666160824162546, PMID 27554807.
- Zhang L, Peng XM, Damu GL, Geng RX, Zhou CH. Comprehensive review in current developments of imidazole-based medicinal chemistry. *Med Res Rev*. 2014;34(2):340-437. doi: 10.1002/med.21290, PMID 23740514.
- Soayed AA, Refaat HM, Noor El-Din DA. Metal complexes of moxifloxacin-imidazole mixed ligands: characterization and biological studies. *Inorg Chim Acta*. 2013;406:230-40. doi: 10.1016/j.ica.2013.04.040.
- Wani MY, Bhat AR, Azam A, Athar F, Sobral AJ. New transition metal complexes containing imidazole rings endowed with potential antimicrobial activity. *Med. Chem Commun*. 2016;7(5):982-9.
- Li B, Webster TJ. Bacteria antibiotic resistance: new challenges and opportunities for implant-associated orthopedic infections. *J Orthop Res*. 2018;36(1):22-32. doi: 10.1002/jor.23656, PMID 28722231.
- Gu J, Wen M, Liang X, Shi Z, Kirillova MV, Kirillov AM. Multifunctional aromatic carboxylic acids as versatile building blocks for hydrothermal design of coordination polymers. *Crystals*. 2018;8(2):83. doi: 10.3390/cryst8020083.
- Akhtar MN, Tahir S, Sadakiyo M, Warsi MF, AlDamen MA, Song Y. An azide-bridged copper (II) 1D-chain with ferromagnetic interactions: synthesis, structure and magnetic studies. *Trans Met Chem*. 2017;42(7):635-41.
- Yue Q, Gao E-Q. Azide and carboxylate as simultaneous coupler for magnetic coordination polymers. *Coord Chem Rev*. 2019;382(1):1-31. doi: 10.1016/j.ccr.2018.12.002.
- Tekiner-Gulbas B, Westwell AD, Suzen S. Oxidative stress in carcinogenesis: new synthetic compounds with dual effects upon free radicals and cancer. *Curr Med Chem*. 2013;20(36):4451-9. doi: 10.2174/09298673113203690142, PMID 23834180.
- Kalarani R, Sankarganesh M, Kumar GGV, Kalanithi M. Synthesis, spectral, DFT calculation, sensor, antimicrobial and DNA binding studies of Co(II), Cu(II) and Zn(II) metal complexes with 2-amino benzimidazole Schiff base. *J Mol Struct*. 2020; 1206127725. doi: 10.1016/j.molstruc.2020.127725.
- O'Shaughnessy M, McCarron P, Viganor L, McCann M, Devereux M, Howe O. The antibacterial and anti-biofilm activity of metal complexes incorporating 3, 6, 9-Trioxaundecanedioate and 1, 10-phenanthroline ligands in clinical isolates of *Pseudomonas aeruginosa* from Irish cystic fibrosis patients. *Antibiotics (Basel)*. 2020;9(10):674. doi: 10.3390/antibiotics9100674, PMID 33027987.
- Ikram M, Rehman S, Subhan F, Akhtar MN, Sinnokrot MO. Synthesis, characterization, thermal degradation and urease inhibitory studies of the new hydrazide based Schiff base ligand 2-(2-hydroxyphenyl)-3-((E)-(2-hydroxyphenyl)methylidene)amino)-2,3-dihydroquinazolin-4(1H)-one. *Open Chem*. 2017;15(1):308-19. doi: 10.1515/chem-2017-0035.
- Ansari IA, Sama F, Shahid M, Ahmad M, Nayab PS, Rahisuddin S *et al*. Synthesis, crystal structures and spectral characterization of Cu(II) and Mn(II) complexes of 4-hydroxy-3-methoxybenzaldehyde: antioxidant properties and molecular docking studies. *J Coord Chem*. 2016;69(22):3336-53. doi: 10.1080/00958972.2016.1232403.
- Rubab M, Akhtar MN, Zierkiewicz W, Michalczyk M, Nadeem R, Shahid M, *et al*. The role of hydrogen bonding in $\pi\cdots\pi$ stacking interactions in Ni(II) complex derived from triethanolamine: synthesis, crystal structure, antimicrobial, and DFT studies. *Res Chem Intermed*. 2019;45(11):5649-64. doi: 10.1007/s11164-019-03927-9.
- Shahid SA, Anwar F, Shahid M, Majeed N, Azam A, Bashir M, *et al*. Laser-assisted synthesis of MnO. 50ZnO. 50Fe₂O₄ nanomaterial: characterization and *in vitro* inhibition activity towards *Bacillus subtilis* biofilm. *J Nanomater*. 2015;2015:Article ID 896185. doi: 10.1155/2015/896185.
- Zuber M, Tabasum S, Jamil T, Shahid M, Hussain R, Feras KS *et al*. Biocompatibility and microscopic evaluation of polyurethane-poly(methyl methacrylate)-titanium dioxide based composites for dental applications. *J Appl Polym Sci*. 2014;131(3):n/a-. doi: 10.1002/app.39806.
- Li Z, Zhou Z, Zhang T, Tang Z, Yang L, Zhang J. Energetic transition metal (Co/Cu/Zn) imidazole perchlorate complexes: synthesis, structural characterization, thermal behavior and non-isothermal kinetic analyses. *Polyhedron*. 2012;44(1):59-65. doi: 10.1016/j.poly.2012.06.030.
- Abdel-Rahman LH, El-Khatib RM, Nassr LAE, Abu-Dief AM. DNA binding ability mode, spectroscopic studies, hydrophobicity, and *in vitro* antibacterial evaluation of some new Fe(II) complexes bearing ONO donors amino acid Schiff bases. *Arab J Chem*. 2017;10(2):S1835-46. doi: 10.1016/j.arabjc.2013.07.010.
- Kiran KR. Synthesis, characterization and antibacterial activity of Cu(II), Zn(II) ternary complexes with maltol and glycylglycine. *Chem Sci Trans*. 2014;3(2):3592-601.
- Rehman F, Mairaj S. Thermodynamic and Biological Studies of Some Bivalent Metal complexes with 2, 4-dihydroxy butyrophenone oxime (DHBOX). *Orientjchem*. 2012;28(1):581-5. doi: 10.13005/ojc/280176.
- Karabasannavar S, Allolli P, Shaikh IN, Kalshetty BM. Synthesis, characterization and antimicrobial activity of some metal complexes derived from thiazole Schiff bases with *in-vitro* cytotoxicity and DNA cleavage studies. *IJPER* 2017;51(3):490-501. doi: 10.5530/ijper.51.3.77.

PICTORIAL ABSTRACT



SUMMARY

In the current study, cobalt and iron-containing complexes were synthesized by using their metal salts with imidazole and carboxylates ligands in MeOH / MeCN. In complexes 1-4, azide is also used as an additional ancillary ligand. These complexes were characterized by FTIR and elemental analyses for their structure elucidation. These complexes were evaluated for antibacterial biofilm inhibition against *S. aureus* and *E. coli* strains. Herein it was observed that complex 3 exhibits remarkable inhibition against *S. aureus* whereas 5 and 2 also shows significant inhibition against *E. coli*. All these complexes (1-5) indicates the cytotoxicity against bovine erythrocytes.

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