RESEARCH ARTICLE

Synthesis and Biological Evaluation of Novel Imidazolone - Thiabendazole-Based Metal Complexes

Chaudhari SR[1], Patil PN[2], Parab YS[3], Pawar NS[4*]

[1]*Department of Chemistry, Shri V. S. Naik, Arts, Commerce and Science College, Raver, India.*
[2]*Department of Applied Science and Humanities and Humanities, R. C. Patel Institute of Technology, Shirpur, India.*
[3]*Department of Basic Science and Humanities, SVKM's Dwarkadas J. Sanghvi College of Engineering, Mumbai, India.*
[4]*Department of Chemistry, Pratap College, Amalner, Maharashtra, India.*

Received: 13th March, 2024; Revised: 24th May, 2024; Accepted: 10th July, 2024; Available Online: 31st August, 2024

ABSTRACT

Thiabendazole-based metal complexes are attracting interest due to their special antimicrobial activities. The current investigation describes the preparation of ligand L1 and its metal complexes [M ($C_{26}H_{17}N_5OS$) Cl_2] M = Co, Ni, Cu and Zn. Mass, ^{1}H-NMR, IR, and UV were used to characterize these compounds. L1 exhibited the highest potency towards many bacteria. It shows the maximum zone of inhibition as compared to any other ligand. Thus, the antibacterial potency of L1 is better as compared to standard drugs. Imidazolone-TBZ ligands L1 are also more susceptible to some bacteria and also show antifungal potency against *Pseudomonas aeruginosa*. The significance of such work triggered the possibility that these ligands L1 and metal complexes can be efficacious drugs against bacterial and fungal species that could be advantageous in designing powerful antibacterial and antifungal compounds for medicinal use. All these synthesized compounds are in addition to the library of heterocyclic compounds.

Keywords: Imidazolone-TBZ ligands, Metal complexes, Antimicrobial activities.

International Journal of Pharmaceutical Quality Assurance (2024); DOI: 10.25258/ijpqa.15.3.27

How to cite this article: Chaudhari SR, Patil PN, Parab YS, Pawar NS. Synthesis and Biological Evaluation of Novel Imidazolone – Thiabendazole-Based Metal Complexes. International Journal of Pharmaceutical Quality Assurance. 2024;15(3):1268-1274.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Oxazolones are heterocyclic compounds that have been around for a long time. They are essential for the production of numerous organic compounds like thiamine,[1] amides,[2] and peptides,[3-5] in addition to many polyfunctional compounds,[6]

The C-2 and C-4 positions of oxazolones are important for the activity of oxazolones.[7] The bond extension in the double bond at C-4 and the phenyl ring at C-2 plays an important role in generating activity.[8] (Figure 1) The phenyl ring at the C-2 position slows down the rate of ring opening of oxazolones.[9]

The production of numerous physiologically active compounds depends on 4-Arylidene-2-phenyl-5-(4H) oxazolones. Oxazolones constitute a significant class of heterocyclic compounds with five members. The synthesis of several chemical molecules, including as amino acids, peptides, and compounds with antibacterial, anticancer, and antitumor activities, depends on these incredibly adaptable intermediates.[10–19]

This chapter covers the preparation, characterization, and assessment of the biological properties of metal complexes based on imidazolone and trimedazole.

It includes synthesis of 5-substituted imidazolones-[2-(4'-thiazolyl)]-*1-H-* benzimidazole ligands L1. Different oxazolones 6, 8 and 10 were intermediates of the above ligands. Oxazolone derivatives were prepared by refluxing *N*-benzoyl glycines and substituted aromatic aldehyde using sodium acetate and acetic anhydride. These oxazolones then treated with 5-amino-[2-(4'-thiazolyl)]-*1H*-benzimidazole to give L1.

Oxazolones also have broad spectrum of biological activities. Oxazolones are large nitrogen-containing heterocycles and show antifungal, antibacterial, anti-inflammatory and anti-HIV activities.

Oxazolone derivatives can be converted into imidazolones simply by reaction with primary amines in pyridine to give corresponding imidazolones.[16] El-Kalyoubi[17] reported preparation of 5 - imidazolones derivatives.

MATERIALS AND METHOD

Synthesis of 5-amino-[2-(4'-thiazolyl)]-1 H-benzimidazole

- Nitration of 2 - (4' - thiazolyl)]- 1 H - benzimidazole

**Author for Correspondence: nileshpawar1329@rediffmail.com*

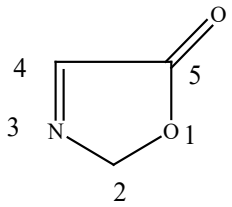


Figure 1: Structure of oxazole-5-one

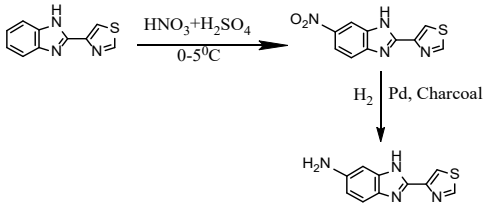


Figure 2: 5-amino-[2-(4'-thiazolyl)]-1H-benzimidazole

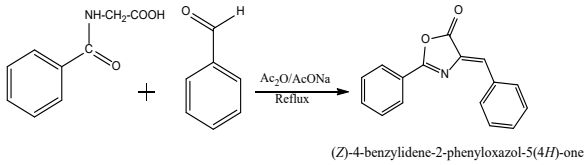


Figure 3: Synthesis of 4-benzylidene-2 phenyloxazol- 5(4H)-one

- Palladium catalyzed reduction of (5-nitro- [2 - (4'-thiazolyl)] – 1 H - benzimidazole)
- To a solution of 2 - (4'- thiazolyl)]- 1H - benzimidazole (24 gm, 0.12 mmol) in cold concentrated H_2SO_4 was added 40 mL concentrated HNO_3 dropwise between 0 to 5°C. After stirring for two hours at room temperature, the mixture was poured into ice water. The faint yellow precipitate separated. Excess acid is then neutralized by $NaHCO_3$. The desired precipitate - (5-nitro- [2-(4'-thiazolyl)]-1H-benzimidazole) obtained was exhaustively washed using ethanol and dried under vacuum to get 59% yield. Observed M. P. was 240 to 242°C (Figure 2). (Reported m. p. 242°C) Thin layer chromatography (TLC) (9:1, ethyl acetate:hexane) was used to track the reaction.
- Five grams (0.02 mmol) of a 5-nitro-[2-(4'-thiazolyl)]-1H-benzimidazole solubilized in 100 mL of absolute ethyl alcohol. Reduction of this solution was done by using one gm of 10% wet palladium-on-charcoal catalyst with 5 kg/cm^2 pressure at room temperature for two hours. When uptake of hydrogen was completed and confirmed, the absence of nitro group was confirmed by TLC (chloroform: methanol 9:1). The catalyst removal was done by filtration, and the solvent evaporated in a vacuum. The precipitate was washed fully using chilled ethyl alcohol and dried under vacuum. Observed M. P. was 231-233 ^{0}C while yield was 58 %. (Figure. 2)

Synthesis of 4 – benzylidene – 2 – phenyloxazol – 5-(4H) - one

Benzaldehyde (1.32 g, 0.0125 mmol), N-benzoyl glycine (2.24 g, 0.0125 mmol), acetic anhydride (3.90 g, 0.04mmol), and anhydrous sodium acetate (1.025 g, 0.0125 mmol) taken in round bottom flask and heated at refluxed condition with constant stirring (4 hours). After cooling the liquid, 25 mL of ethanol was gradually added. Let the mixture stand for 14 hours. Filtered the product and gave washing first with hot water and subsequently by 1:1 ice-cold methanol. The precipitate was dried and recrystallized with ethanol. The reaction's progress was monitored with TLC (9:1, chloroform:methanol). The pure product obtained had a yield of 70% and a melting point of 165 to 167°C (Figure 3).

Synthesis of L1 i.e. 4-benzylidene-2-phenyl-1 - (2 - (thiazol – 4 - yl) - 1Hbenzimidazole-5-yl)-1H – imidazole - 5(4H)-one

Solution of oxazolone derivative 6 (0.02 mmol, 4.98 g) and 5 – amino thiabendazole 3 (0.02 mmol, 4.32 g) in pyridine refluxed around 16 hours. After completion of the reaction (TLC 9:1, Chloroform: Methanol) the mixture was evaporated using a rota evaporator. In 100 mL water was then added to the residue and added dilute HCl solution till pH 6 to 7 value. Filtered the precipitate and washed with water and dried (50–60°C). About 100 mL ethyl alcohol and the product heated to get clear solution. The reaction mixture was filtered in a heated environment after 0.5 g of carbon was added. Next, pour 100 mL of water into this filter and let it sit at room temperature for two hours, stirring. By filtering, the product was eliminated. The light yellow-colored precipitate was dried (50–60°C, 8 hours). 81 % yield was obtained with M.P. 188–190°C. (Figure 4)

Reactions of L1 with various metal chlorides

Synthesis of [Co($C_{26}H_{17}N_5OS$)Cl_2] (1a)

The cobalt chloride ($CoCl_26H_2O$, 0.4 g, 1.78 mmol) was dissolved in ethyl alcohol and then 30 mL of hot ethanolic solution of L1(0.8 g,1.78 mmol,4-benzylidene-2-phenyl-1-(2-(thiazol-4-yl)-1H benzimidazole - 5 - yl) – 1 H - imidazol-5-(4H) - one) was added slowly. The above solution refluxed for 4.5 hours. A light green powder separated after being an overnight. The precipitate was washed with cold ethyl alcohol and dried (Yield 62%, M.P. 297–299°C).

Similarly, all metal complex are prepared.

General reaction scheme and structure for the formation of metal complexes from ligands L1 are shown in Figures 5 and 6, respectively as given below-

Where M: L as 1:1

L = L1

M = Co, Ni, Cu and Zn

X = Chloride ion

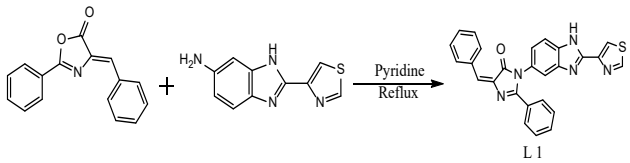


Figure 4: 4-benzylidene-2-phenyl-1 - (2 - (thiazol – 4 - yl) - 1Hbenzimidazole-5-yl) - 1H-imidazol – 5 - (4H)-one (L1)

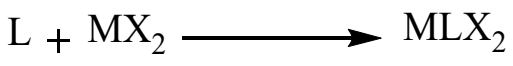


Figure 5: General reaction scheme for formation of metal complexes from ligands L1

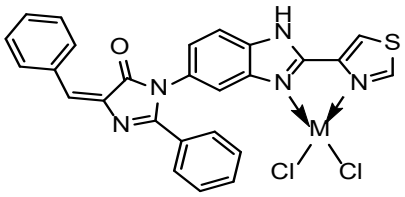


Figure 6: Structure of metal complex with Ligand L1

RESULTS AND DISCUSSION

Synthesis of 5-amino-[2 - (4'- thiazolyl)] – *1 H* - benzimidazole

Nitration of 2 - (4'-thiazolyl)]- 1H-benzimidazole

The desired precipitate 2 **(**5-nitro-[2-(4'-thiazolyl)]-*1H*-benzimidazole) was obtained, gave washing with ethyl alcohol and dried to get 59% yield. Observed M. P. was 240 to 242°C**.** (Reported m. p. 242°C) The reaction was monitored using TLC (9:1, ethyl acetate:hexane).

- *IR Characterization (KBr) in (cm^{-1})*

Prominent bands at 3101(N-H stretching) and 1095 (N-H vibration), 1573 was obtained for $\mathbf{V}_{(C = N \text{ for imidazole})}$, and 1473 $\mathbf{V}_{(C = N \text{ for thiazole})}$. While 1519 and 1342 due to asymmetric and symmetric stretching vibrations due to N-O bonds, shown in Table 1.

- Synthesis of 5-amino-[2-(4'-thiazolyl)]-*1H*-benzimidazole
- Observed M. P. was 231–233°C while yield was 58 %. IR Characterization (KBr) in (cm^{-1}): 3116, 3194, 3302 (due to N-H stretching), 1496 $\mathbf{V}_{(C = N \text{ imidazole})}$, 1411 $_{(C = N \text{ thiazole})}$, 1357 C - S stretch. LCMS*(m/z)* by Mass**:** 239, 218.02, 217.2, 213.2, 157.1, 107.1, 85.1.

The mass spectrum of 5-amino-2-(thiazol-4-yl)-*1H*-benzimidazole shows ion [$C_{10}H_8N_4S$ + Na]*(m/z)* 239 and molecular ion [$C_{10}H_8N_4S$ + 1] at *(m/z)* = 217.2 which corresponds to molecular weight.

Synthesis and characterization of Imidazolone-TBZ Ligands L1,

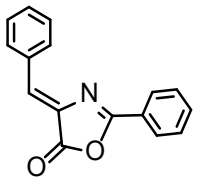
Synthesis and characterization of ligand L1

L1 is [4-benzylidene-2-phenyl- 1 - (2 - (thiazol-4 - yl) - *1H* - benzimidazole-5 - yl) - *1H*-imidazol-5(4*H*) - one]

Preparation of 4 – benzylidene – 2 – phenyloxazol - 5(4*H*) - one

The melting point of a product as shown in Figure 7 was obtained 165 to 167°C and the yield was 70%.

IR Characterization (KBr) in cm^{-1}: 3055 (due to aromatic C-H stretch), 1789 (due to C=O stretch), 1651 (C=N stretch), 1157 (C-O stretch), 763 and 686 (deformation of monosubstituted benzene) shown in Table 1.



(*Z*)-4-benzylidene-2-phenyloxazol-5(4*H*)-one

Figure 7: 4 – benzylidene – 2 – phenyloxazol – 5 - (4*H*) - one

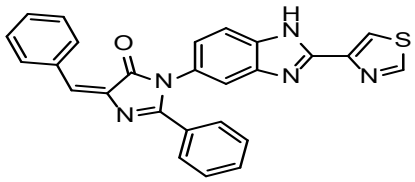


Figure 8: 4-benzylidene-2-phenyl- 1- (2 - (thiazol – 4 - yl) - 1H-benzimidazole - 5 - yl) - 1H - imidazol 5-(4H) one (L1)

Synthesis of L1 i.e. 4-benzylidene-2-phenyl-1 - (2 - (thiazol – 4 - yl) - *1H*-benzimidazole-5-yl)-*1H*-imidazol-5(4*H*) - one L1.

The light yellow-colored precipitate (Figure 8) dried around 50 to 60°C about 8 hours (Yield 81% M. P. 188–190°C).

IR Characterization (KBr) (cm^{-1})

3363 (N-H stretching), 1639 (carbonyl stretching of amide), 1477, (C=N stretch of imidazole), 1435 (C=N stretch of thiazole), 1284 (C-S stretching) shown in Table 1.

^{1}H-NMR (300 MHz, DMSO - d6, δ ppm)

10.21 (s, 1H), 9.31 (s, 1H), 8.024-8.39(m, 5H), 7.19-7.65 (m, 10H).

Mass by LCMS (m/z)

For $C_{26}H_{17}N_5OS$+H *(m/z)* 448.1 (calculated 447.5), [$C_{10}H_8N_4S$ + 1] at *(m/z)* = 217.01

Comparison of IR Frequencies of Ligands L1 with TBZ and 5-amino-[2-(4'-thiazolyl)]-*1H*-benzimidazole

Results are depicted in Table 1.

Preparation and characterization of transition metal complexes of ligands L1 as shown in Figure 6.

Reactions of L1 with various metal chlorides

Synthesis of [Co ($C_{26}H_{17}N_5OS$)Cl_2] (1a)

Table 1: Comparison of IR data for TBZ, 5-aminoTBZ with ligands L1

IR	*T B Z cm^{-1}*	*5 - NH_2 – T B Z cm^{-1}*	*L - 1 cm^{-1}*
N - H	3093	3116	3093
N - H	1095	-	1095
$\upsilon_{(C = N) \text{ imidazole}}$	1589	1496	1481
$\upsilon_{(C = N) \text{ thiazole}}$	1419	1411	1404
C - S	1296	1357	1292
- C = O	-	-	1639

Solubility

Insoluble in the following solvents water, ethanol, methanol and soluble in DMSO solvent.

UV (λ_{max}, DMSO): 253, 286, 422 nm

IR (KBr, cm $^{-1}$): 3093 (N - H stretch), 1095 (N - H vibration), 1639 (C=O stretch of amide), 1481 (C=N stretch of imidazole), 1404 (C=N stretch of thiazole), 1292 (C-S stretch of thiazole).

Mass by LCMS (*m/z*):578 (M+1) corresponds to molecular weight, 507, 448 ($C_{26}H_{17}N_5OS$), 217 ($C_{10}H_8N_4S$+1).

Synthesis of [Ni($C_{26}H_{17}N_5OS$)Cl_2] (1b)

The precipitate was washed with cold ethyl alcohol and dried. (Yield = 54%, M.P. 278–280°C) shown in Table 2.

Characterization of 1b [Ni($C_{26}H_{17}N_5OS$)Cl_2]

Solubility: Insoluble in solvents such as water, ethanol, methanol but dissolve with DMSO.

UV (λ_{max}, DMSO): 253, 277, 425 nm

IR (KBr, cm^{-1}): 3097 (N - H stretch), 1639 (-C = O stretch), 1477(C = N)$_{imidazole}$, 1438(C = N)$_{thiazole}$, 1280 (C - S stretch), 999, 925, 810, 694, 432, 370.

Mass by LCMS (*m/z*): 576, 505, 446, 385, 215, 154. The mass spectra of the ligand and its metal complexes showed molecular ion peaks at m/z 576 and 446 ($C_{26}H_{17}N_5OS$), respectively, which were ascribed to M and the ligand.

Synthesis of [Cu ($C_{26}H_{17}N_5OS$) Cl_2] (1c)

The precipitate gave washings with chilled ethyl alcohol and dried. (Yield 48% with Melting point 279–281°C) as shown in Table 2.

Characterization of 1c [Cu ($C_{26}H_{17}N_5OS$) Cl_2]

Solubility: Insoluble in solvents such as water, ethanol, and methanol but obtained clear solution with DMSO.

UV (λ_{max}, DMSO): 251, 287, 322 nm

IR (KBr, cm^{-1}): 3093 (N-H stretch), 1635 (-C=O stretch), 1477 (C=N)$_{imidazole}$, 1435 (C=N)$_{thiazole}$, 1280 (C-S stretch), 999, 810, 690, 435, 366.

Mass by LCMS (*m/z*):583 [Cu ($C_{26}H_{17}N_5OS$) Cl_2 + 1], 556, 446 [($C_{26}H_{17}N_5OS$]

Synthesis of [Zn ($C_{26}H_{17}N_5OS$)Cl_2] ,(1d)

The product gave washings with cold ethyl alcohol and subsequently dried to give a yield 51% with M.P. 242–244°C as shown in Table 2.

Characterization of 1d i.e. [Zn($C_{26}H_{17}N_5OS$)Cl_2]

Solubility: Insoluble in solvents such as water, ethanol, and methanol but formed homogeneous solution with DMSO.

UV (λ_{max}, DMSO): 225, 287, 455 nm

IR (cm^{-1}, KBr): 3093 (N - H stretch), 1639 (-C = O stretch), 1477(C = N)$_{imidazole}$, 1438(C = N)$_{thiazole}$, 1280 (C - S stretch), 1203, 999, 810, 756, 690, 432, 366 shown in Table 3.

Mass by LCMS (*m/z*): 585 [Zn ($C_{26}H_{17}N_5OS$) Cl_2+1], 449 [$C_{26}H_{17}N_5OS$+1], 386, 250, 217 ($C_{10}H_8N_4S$+1).

Analytical data of metal complexes of L1 (4-benzylidine- 2 -phenyl-1- (2-(thiazol -4-yl) - ***1H-*** benzimidazol-5-yl)-***1H-*** imidazole - 5 - one)

Table 2: Analytical data of metal complexes 1a, 1b, 1c, 1d

Compound	*Mol. formula*	*Mol. wt.*	*Color*	*M.P. (°C)*	*Yield (%)*
1a	[Co($C_{26}H_{17}N_5OS$) Cl_2]	577.35	Light green	297-299	62
1b	[Ni($C_{26}H_{17}N_5OS$) Cl_2]	577.11	Light yellow	278-280	54
1c	Cu($C_{26}H_{17}N_5OS$) Cl_2]	581.96	Yellow	279-281	48
1d	[Zn($C_{26}H_{17}N_5OS$) Cl_2]	583.81	Reddish brown	242-244	51

Table 3: Comparison of IR data of L1 with metal complexes 1a, 1b, 1c, 1d

IR band	*L1 cm $^{-1}$*	*1a cm^{-1}*	*1b cm $^{-1}$*	*1c cm $^{-1}$*	*1d cm $^{-1}$*
N-H stretch	3093	3363	3097	3093	3093
$\upsilon_{(C=N)imidazole}$	1481	1477	1477	1477	1477
$\upsilon_{(C=N)thiazole}$	1404	1435	1438	1435	1438
C-S stretch	1292	1284	1280	1280	1280
-C=O stretch	1639	1639	1639	1635	1639

Comparison of IR Frequencies of Ligands and their Metal Complexes

Results are depicted in Table 3.

Magnetic moment and molar conductivity of metal complexes

Magnetic moment values provide information about the structure of metal complexes. It gives a number of unpaired electrons present in metal complexes. Cobalt complexes with one unpaired electron may be octahedral or square planar. The cobalt ion has 3d7 electrons. The observed magnetic moment for cobalt ion is in the range of 1.60 to 1.70 shown in Table 4.

This value supports that cobalt complexes are square planar structures. Nickel and zinc complexes do not show magnetic moment. They are diamagnetic in nature. In contrast, copper complexes exhibit the magnetic moment of one unpaired electron. From detail analysis and magnetic moment study, Ni (II) and Zn (II) might have tetrahedral structures, whereas Co (II) and Cu (II) might have square planar structures.

Thermo gravimetric analysis of metal complexes

Table 5 shows the thermal decomposition data of the metal complexes [Ni($C_{26}H_{17}N_5OS$)Cl_2]. From thermal studies % of

Table 4: Molar conductivities and magnetic moments of metal complexes of L1

Metal complex	*Formula*	*Molar conductivity in DMSO Λ_M ($ohm^{-1}cm^2mol^{-1}$)*	*Magnetic moment (B. M.) $\mu_{eff.}$*
1a	[Co($C_{26}H_{17}N_5OS$)Cl_2]	47.76	1.65
1b	[Ni($C_{26}H_{17}N_5OS$)Cl_2]	48.00	----
1c	[Cu($C_{26}H_{17}N_5OS$)Cl_2]	43.31	1.71
1d	[Zn($C_{26}H_{17}N_5OS$)Cl_2]	36.41	----

Table 5: Thermal decomposition data of the metal complex 1b [$Ni(C_{26}H_{17}N_5OS)Cl_2$]

Metal complex	*Stages*	*Temp. range TG (°C)*	*Mass loss from thermo gram (%)*		*Decomposition pattern*
			Expt. loss (%)	*Theor. loss (%)*	
1b [$Ni(C_{26}H_{17}N_5OS)Cl_2$]	1	55 to 120	14.28	15.77	2 HCl, H_2O
	2	120 to 330	18.19	18.33	Loss of part of ligand
	3	330 to 800	55.97	52.95	Loss of part of ligand
	4	800 to 1000	88.44	87.05	[$Ni(C_{26}H_{17}N_5OS\ Cl_2)$] to NiO

Table 6: Antimicrobial activities for ligand L1 ($C_{26}H_{17}N_5OSCl_2$) and metal complexes

S. No.	*Sample code*	*Inhibitory zone (Diameter in mm)*						
		G^+ bacteria		*G^- bacteria*		*Fungi*		
		S. a.	*B. s.*	*E. c.*	*P. a.*	*C. a.*	*A. n*	*F. m.*
1	L1	35.54	34.59	38.20	34.35	----	----	----
2	1a	11.89	7.64	11.50	-----	8.42	-----	------
3	1b	7.80	7.13	9.53	-----	10.47	------	7.30
4	1c	7.71	19.13	8.01	------	-----	-----	-------
5	1d	7.67	11.12	10.24	-------	------	-----	-----
6	A	27.90	20.05	26.91	14.10	NA	NA	NA
7	B	NA	NA	NA	NA	20.15	7.98	8.10

1a: [$Co(L1)Cl_2$] **1c:**[$Cu(L1)Cl_2$] **A**:Chloramphenicol
1b: [$Ni(L1)Cl_2$] **1d:**[$Zn(L1)Cl_2$] **B**:Amphotericin

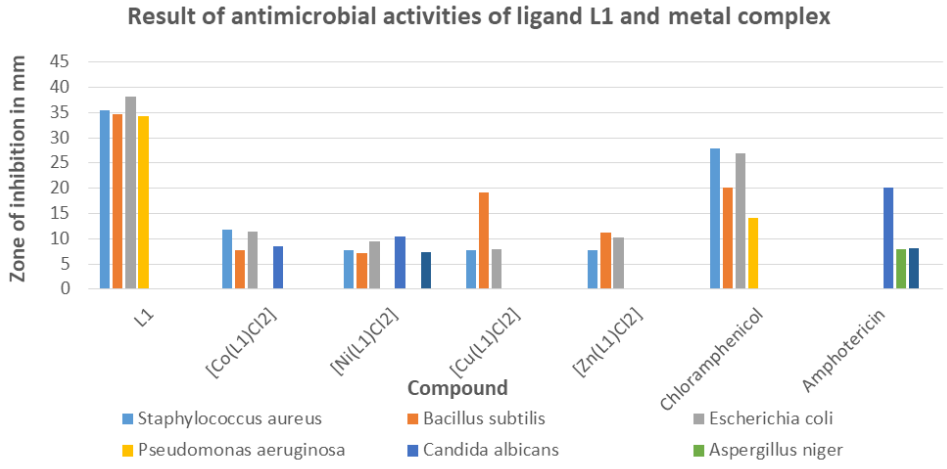


Figure 9: Comparison of zone of inhibition of L1 and its metal complex

metal was found to be inconsistent with the calculated values of studied metal complexes. The thermal data aided the structure of complexes as [MLX2], where L = L1 and M = Co(II), Ni(II), Cu(II), and Zn(II). The final product of decomposition are identified as oxides like CoO, NiO, CuO and ZnO. The metal complexes did not show any appreciable change till 100°C when heated, indicating the absence of water of hydration.

Evaluation of Antimicrobial Activities

Prepared compounds were checked for their potential antimicrobial activities such as antibacterial activities using

Table 7: %Antioxidant activities of ligand L1 and its metal complexes

Sample code	*Ligands and metal complexes*	*%DPPH radical scavenging/ antioxidant activities*
L1	($C_{26}H_{17}N_5OS$)	44.52
1a	[$Co(L1)Cl_2$]	45.65
1b	[$Ni(L1)Cl_2$]	28.94
1c	[$Cu(L1)Cl_2$]	44.26
1d	[$Zn(L1)Cl_2$]	**79.56**
Standard	Ascorbic acid	94.00

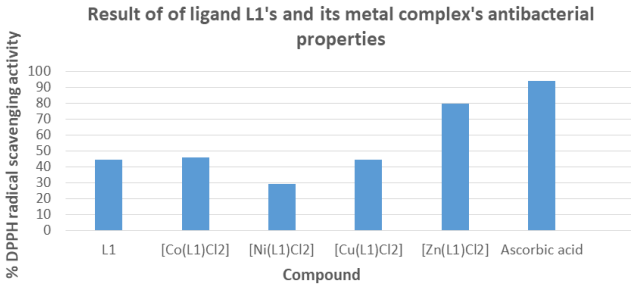


Figure 10: Metal complexes and ligand L1's antioxidant properties

microorganisms *Staphylococcus aureus, Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli, Aspergillus niger, Candida albicans,* and *Fusarium moniliforme*. The assay was carried out at 100 µg/disc concentration. L1 exhibited the highest potency towards many bacteria. It shows the maximum zone of inhibition as compared to any other ligand as shown in Table 6 and Figure 9. Thus, the antibacterial potency of L1 is better as compared to standard drugs. Imidazolone-TBZ ligands L1 are also more susceptible to some bacteria and also show antifungal potency against *P. aeruginosa*.

Evaluation of Antioxidant Activities

1,1-diphenyl-2-picrylhydrazyl or 2,2-diphenyl1-picrylhydrazyl (DPPH) was used to test the scavenging capacity of ligands L1 and their metal complexes. All the synthesized metal complexes show more antioxidant activities as compared to their ligands. But all synthesized compounds, i.e., ligands L1 and corresponding metal complexes, are less antioxidant than standard ascorbic acid used. Among the four metals used, generally, zinc metal complexes of L1 possess more antioxidant activity, while nickel and copper metal complexes of L1 show poor antioxidant activity (as shown in Table 7 and Figure 10).

CONCLUSION

In conclusion, we have developed derivatives of 5-substituted - [2-(4'-thiazolyl)]-1H-benzimidazole ligands (L1), which demonstrated elevated selectivity and sensitivity towards metal ions. The various transition metal complexes were produced by mixing ligands in an ethanolic solution at a 1:1 molar ratio with the relevant transition metal chlorides. Several spectroscopic and analytical techniques were used to characterize the potential structures of ligands L1 and their metal complexes. Every synthesized ligand and metal complex was assessed, confirming its antioxidant, antifungal, and antibacterial properties. Against every strain tested, the majority of the ligands and metal complexes showed good to moderate antibacterial and antifungal activity. From antimicrobial data we have concluded that L1 and corresponding metal complexes showed excellent activity as compared to the standard antibacterial drugs. Moreover, biological screening shows that some metal complexes enhance the activity against bacteria and fungi more than corresponding ligands. The significance of such work triggered the possibility of prepared ligands and metal complexes might be more effective drugs against bacterial and fungal species. This might be useful in creating effective antifungal and antibacterial drugs for medical applications. All these synthesized compounds are in addition to the library of heterocyclic compounds.

REFERENCES

1. Ismail MI. Physical Characteristics and Polarographic Reduction Mechanism of Some Oxazolones. Canadian Journal of Chemistry. 1991;69(12):1886–1892.DOI:10.1139/v91-273
2. Park BS, Oh CM, Chun KH, Lee JO. Photoinduced One Pot Transformation of 2-phenyl-4-ethylidene-5(4H)-oxazolone and Allylic Alcohols to γ, δ-unsaturated N-benzoyl amides. Tetrahedron Letters. 1998;39(52):9711–9714. DOI:10.1016/s0040-4039(98)02232-1
3. Palcut M. Spectral Properties of Novel 1, 3-oxazol-5(4H)-ones With Substituted Benzylidene and Phenyl Rings. Acta Chimica Slovenica. 2009. DOI:https://acta-arhiv.chem-soc.si/56/56-2-362.pdf
4. Seebach D, Jaeschke G, Gottwald K, Matsuda K, Formisano R, Chaplin DA, et al. Resolution of Racemic Carboxylic Acid Derivatives by Ti-TADDOLate Mediated Esterification Reactions—A general Method for the Preparation of Enantiopure Compounds. Tetrahedron. 1997;53(22):7539–7556. DOI:10.1016/s0040-4020(97)00456-0
5. Gottwald K, Seebach D. Ring Opening with Kinetic Resolution of Azlactones by Ti-TADDOLates. Tetrahedron. 1999;55(3):723–738. DOI:10.1016/s0040-4020(98)01064-3
6. Matsunaga H, Ishizuka T, Kunieda T. Synthetic Utility of Five-membered Heterocycles—Chiral Functionalization and Applications. Tetrahedron. 2005;61(34):8073–8094. DOI:10.1016/j.tet.2005.05.076
7. Abdel-Aty AS. Pesticidal Effects of Some Imidazolidine and Oxazolone Derivatives. World Journal of Agricultural Sciences. 2009:5,105-113. DOI: https://citeseerx.ist.psu.edu/document?repid=rep1&type=pdf&doi=727818afaf489c698884df5c390ef47316e961b1
8. Khan KM, Mughal UR, Khan MTH, Zia-Ullah, Perveen S, Iqbal Choudhary M. Oxazolones: New Tyrosinase Inhibitors; Synthesis and Their Structure–Activity Relationships. Bioorganic & Medicinal Chemistry. 2006;14(17):6027–6033. DOI: 10.1016/j.bmc.2006.05.014
9. Betłakowska B, Banecki B, Czaplewski C, Łankiewicz L, Wiczk W. Reaction of 4-benzylidene-2-methyl-5-oxazolone with Amines, Part 2: Influence of Substituents in Para-position in the Phenyl ring and a Substituent on Amine Nitrogen Atom on the Reaction Kinetics. International Journal of Chemical Kinetics. 2002;34(3):148–55. DOI: 10.1002/kin.10039
10. Mistry RN, Desai KR. Studies on Synthesis of Some Novel Heterocyclic Azlactone Derivatives and Imidazolinone Derivatives and Their Antimicrobial Activity. E-Journal of Chemistry. 2005;2(1):42–51. DOI:10.1155/2005/542938
11. Pawar NS, Patil PN, Pachpande RN. An Efficient Synthesis and Antibacterial Activity of Some Novel 3,4–dihydropyrimidin-2-(1H)-ones. Chemical Proceedings. 2021;8,37. DOI:10.3390/ecsoc 25 11720
12. Patil JU, Patil PN, Pawar NS. Synthesis and Antibacterial Activity of Thymyl Ethers. Chemical Proceedings; 2022;8,57. DOI:10.3390/ecsoc 25 11747
13. Bendre RS, Patil RD, Patil PN, Patel HM, Sancheti RS. Synthesis and Characterization of New Schiff-Bases as Methicillin Resistant Staphylococcus Aureus (MRSA) Inhibitors. Journal

of Molecular Structure. 2022;1252,132152. DOI:10.1016/j.molstruc.2021.132152

14. Jawarkar SG, Game MD. Synthesis, Characterization and Antimicrobial Evaluation of New Substituted Thiazolidinones Bearing Triazole Moiety. International Journal of Pharmaceutical Quality Assurance. 2024; 15(2):796–802. DOI:10.25258/ijpqa.15.2.39
15. Verma G, Verma P, Srivastava A, Yadav AK. Evaluation of Antiviral, Antibacterial and Antioxidant Activity of Morinda tinctoria Roxb., Abroma augusta L. Educes and Myristica fragrans Houtt. Ethereal Oil in Microcapsules. International Journal of Pharmaceutical Quality Assurance. 2024;15(02):689–697. DOI: 10.25258/ijpqa.15.2.22
16. Chaudhari SR, Patil PN, Patil UK, Patel HM, Rajput JD, Pawar NS, et al. Green Synthesis of N-substituted Benzimidazoles: The Promising Methicillin Resistant Staphylococcus Aureus (MRSA) Inhibitors. Chemical Data Collections. 2020;25(100344):100344. DOI:10.1016/j.cdc.2020.100344
17. El-Kalyoubi S, Agili F, Zordok WA, El-Sayed ASA. Synthesis, In Silico Prediction and In Vitro Evaluation of Antimicrobial Activity, DFT Calculation and Theoretical Investigation of Novel Xanthines and Uracil Containing Imidazolone Derivatives. International Journal of Molecular Science. 2021;22(20):10979. DOI: 10.3390/ijms222010979
18. Shraddha RS, Kumar B, Neeraj SK, Manmohan S, Swati A. In-vitro Analysis of Antioxidant, Anti-Inflammatory, Antidiabetic and Antimicrobial Studies of Kaempferol Ethosomes. International Journal of Drug Delivery Technology. 2024;14(1):118-125. DOI:10.25258/ijddt.14.1.17
19. Shafeeq AA, Hamandi ZMA, Mohammed HM, Ghassan Al-Shamma. Synthesis, Characterization and Evaluation of Antimicrobial Activity for New Nitroimidazole Derivatives. International Journal of Drug Delivery Technology. 2022;12(2):495-501. DOI:10.25258/ijddt.12.2.6