



Evaluation of antimicrobial and insect repellent properties of two novel Zinc (II), and Nickel(II) Complexes containing a tetradentate Schiff Base

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ABSTRACT

Schiff bases and their metal complexes are known to have interesting applications in the field of medicine and also in agriculture as they are reported to have antibacterial, antifungal, anticancer, anthelmintic, analgesic, anti-inflammatory, antiparasitic and antioxidant property. Keeping in view of the pronounced biological activity of the metal complexes of Schiff bases, this study report the synthesis and characterization of transition metal (Zn and Ni) complexes of new Schiff bases and investigation of their antimicrobial, antifungal and insecticidal activities. The complexes have been characterized by spectroscopic and physicochemical studies. Antimicrobial study showed that nickel complex had higher antibacterial and antifungal effect in comparison to zinc complex. Again Gram positive bacteria were found to more susceptible to the nickel complexes than the Gram negative bacteria. The metal complexes had moderate effect in human pathogenic fungus *Candida albicans*. Zn complexes had strong repellent action against both stored grain insect species *T. castaneum* and *C. maculatus*.

Keywords: Metal, Tetradentate Schiff base, Spectroscopic study, Antimicrobial activity, Insect repellent activity

INTRODUCTION

Due to increase of multi-drug resistant microbial pathogens in the last decades, the treatment of infectious diseases becomes a challenging problem. In spite of a large number of antibiotics and chemotherapeutics available for medical use, at the same time the emergence of old and new antibiotic resistance reveals an urgent need for new classes of antimicrobial agents. Some metals have been used as drugs and diagnostic agents to treat a variety of diseases. Platinum compounds such as cisplatin, carboplatin, gold drugs such as myocrisin can be cited in this regard. The field of bioinorganic chemistry, which deals with the study of role of metal complexes in biological systems, has opened a new horizon for scientific research in coordination compounds. Schiff bases derived from amino and carbonyl compound comprise an important class of ligands that easily coordinate

to metal ion via azomethine linkage.¹ Design and synthesis of polydentate Schiff bases and their metal complexes having novel structural features and unusual physico-chemical properties have considerable importance in biological processes² as the Schiff bases show a diversified biological properties including antibacterial, antifungal, herbicidal and antitumor³⁻⁹ due to have their azomethine linkage¹⁰ and also has potential applications as pesticides and insecticides.^{11,12} Transition metal ions play a vital role in a vast number of widely different biological processes¹³ and their activity can be enhanced when the transition metal ions are coordinated to a Schiff base ligand.¹⁰ In recent years, the metal complexes with tridentate S, N, N types have attracted the attention of chemist because of their applications found in the field of pesticides and medicine. In the last decade, a large number of bimetallic Schiff base complexes of different structural types have been synthesized and characterized.^{14,15} Recently, wide varieties of Co(II) Ni(II), Cu(II) and Zn(II) complexes of Schiff base derivatives including compartmental and macrocyclic ligands were tested in vitro for their antibacterial activities against human pathogenic bacteria¹⁶⁻¹⁸ and for cytotoxic activity^{19,20} where the metal complexes have higher antimicrobial activity than the free ligands. Transition metals like Nickel and Zinc has been coordinated with tridentate Schiff base ligand derived from salicylaldehyde and 2-aminobenzimidazole²¹ from indole-3-carboxylaldehyde and m-aminobenzoic acid²² and with bidentate ligand derived from 2,4-dihydroxyacetophenone and p-phenylene diamine²³ has been reported. From literature search, it appears that no work

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has been done on Ni and Zn metal complexes of tetradentate Schiff base derived from glyoxal and 2 aminothiophenol.

In the present work, we have reported the synthesis of a Schiff base ligand H₂L [{2, 2'-(1E, 2E)-ethane-1,2-diylidenedi (E) azanylylidene] dibenzenethiol}] and its novel metal complexes such as [Zn(HL)(NCS)] and [Ni(H₂L)(NCS)₂] and characterization of the ligand and metal complexes by IR and NMR spectroscopy and tested against bacteria and fungus with the main aim to investigate if the novel compounds are potent antimicrobial agents as well as to make a comparison of their biological activities. In addition, an attempt has been made to study the repellent activity of the newly synthesized complexes against two stored grain insect pests as little information is available about the insecticidal properties of such complexes.

MATERIALS AND METHODS

Chemicals

All the chemicals and solvents used in the syntheses were of reagent grade and used as received without further purification. Elemental analyses were carried out on a Perkin-Elmer 2400-II elemental analyzer. The infrared spectra were recorded on a Perkin-Elmer Spectrum 65 FT-IR spectrophotometer with KBr discs (4000–400 cm⁻¹). ¹H NMR spectra of compounds and ligand were recorded with a Bruker DRX500 using CDCl₃ as solvent. Melting point/decomposition temperature was determined with a Mettler FP62 melting point analyzer. Analytical and physical data of ligand and their complexes are presented in Table 1.

Table 1. Physical measurements and analytical data of the ligand and metal (II) complexes (1&2)

Compound	Mol. formula	M.P (°C)	Yield (%)	Found (Calc)%			
				C	H	S	N
Ligand	H ₂ L	95	83	61.73	4.44	23.54	10.28
Zn complex	[Zn(HL)(SCN)]	115	66	45.63	2.81	24.36	10.64
Ni complex	[Ni(H ₂ L)(NCS) ₂]	131	62	42.97	2.70	28.68	12.53

Synthesis of ligand

H₂L [{2, 2'-(1E, 2E)-ethane-1, 2-diylidenedi (E) azanylylidene] dibenzenethiol}]

2-aminothiophenol (1gm, 8 mmol) was added to a solution of glyoxal (0.232gm, 4 mmol) in methanol (50 ml). The mixture was refluxed for six hours and cooled to room temperature. The volume was reduced to approximately 10 ml and the solution was stored overnight. The orange red precipitate that formed was separated and dried. MP. 95°C IR: 417.95cm⁻¹, 455.99cm⁻¹, 728.68 cm⁻¹, 749.13 cm⁻¹, 1685.54 cm⁻¹, 2075.43 cm⁻¹, 3367.17 cm⁻¹. ¹H NMR: δ 1.61, δ 5.23, δ 6.5, δ 8.16.

Synthesis of complexes

Synthesis of compound 1 [Zn(HL)(SCN)]

Methanolic solution (20ml) of Schiff base (0.272gm, 1 mmol) was added to a methanolic (20 ml) solution of zinc perchlorate hexahydrate (0.372gm, 1 mmol) with constant stirring, followed by the addition of a methanolic (5ml) solution of NH₄SCN (0.078gm, 1 mmol). Stirring was continued for further half an hour and the solution was left as such for slow evaporation. Fine crystalline compound 1 was obtained after 14 days. MP 115°C. IR: 422.45 cm⁻¹, 457.48 cm⁻¹, 529.93 cm⁻¹, 729.99 cm⁻¹, 762.97 cm⁻¹, 1618.8 cm⁻¹, 2075.43 cm⁻¹, 3467.37 cm⁻¹. ¹H NMR: δ 1.58, δ 8.18, δ 7.5, δ 9.3, δ 8.0.

Synthesis of compound 2 [Ni(H₂L)(NCS)₂]

Compound 2 was synthesized in the same way as previous compounds. In this case the metal perchlorate used was nickel perchlorate hexahydrate (0.365gm, 1 mmol). Compound 2 was found to be formed after 13 days. MP: 131°C. IR: 421.09 cm⁻¹, 463.23 cm⁻¹, 531.30 cm⁻¹, 730.27 cm⁻¹, 762.29 cm⁻¹, 1621.9 cm⁻¹, 2098.6 cm⁻¹, 3435.16 cm⁻¹. ¹H NMR: δ 1.56, δ 7.5, δ 8.17, δ 7.985.

Microbial strains

Freeze dried microbial culture were purchased from Institute of Microbial Technology, Chandigarh (MTCC) and microbial culture were revived according to the recommended growth medium and recommended temperature. The fungal microorganisms chosen to test antimicrobial activity of the synthesized compounds were *Candida albicans* (MTCC 183) and *Aspergillus niger* (MTCC 10180). On the other hand two Gram positive bacteria *Bacillus subtilis* (MTCC 441) and *Staphylococcus aureus* (MTCC 96) and two Gram negative bacteria *Klebsiella pneumoniae* (MTCC 39) and *Proteus mirabilis* (MTCC 425) were used as the bacterial microorganism. Muller-Hinton agar (Himedia, Mumbai, India) was used for growing bacterial cultures. Sabouraud dextrose agar (Himedia, Mumbai, India) was used for the growth of *Candida albicans* and potato dextrose agar (Himedia, Mumbai, India) was used for the growth of *A. niger*. The ligand and its complexes were water insoluble.

Antimicrobial screening

The standardized disc agar diffusion method²⁴ was applied to determine the activity of the new compounds against the sensitive organism. Briefly, a suspension of the test microorganism (2 × 10⁸ CFU/ml adjusted to 0.5 McFarland Standard) was spread on the solid media plates. The tested compounds were dissolved in dimethylsulfoxide (DMSO) to get concentration of 2 mg/ml. Uniform size (6mm diameter) sterile filter paper disc (Himedia, Mumbai, India) (3 discs per compound) were impregnated by equal volume (10µl) from the specific concentration of dissolved test compounds and carefully placed on inoculated agar surface. Gentamicin disc (Himedia, Mumbai, India) was used as a standard reference in case of bacteria while Fluconazole disc (Himedia, Mumbai, India) was used as a standard antifungal reference and DMSO were used as negative control as they have no inhibition activity. After incubation for 24 hrs at 37°C in case of bacteria and for 48 hrs at 30°C in the case of fungi, inhibition of the organism evidenced by class zone surround each disc was measured and used to calculate mean of inhibition zones (mm).

The activity of test compounds were categorized as i) low activity= mean zone diameter $\leq 1/3$ of the mean zone diameter of control ii) intermediate activity= mean zone diameter $\leq 2/3$ of the mean zone diameter of control and iii) high activity= mean zone diameter $\geq 2/3$ of the mean zone diameter of control.

Determination of minimum inhibitory concentration (MIC)

The minimal inhibitory concentration (MIC, mg/mL) of the compounds were estimated by broth microdilution method^{25,26} against the bacterial strain. All tests were performed in Muller Hinton broth (Himedia, Mumbai, India). A serial dilution of metal complexes (dissolved in DMSO) were prepared in a 96 well microtiter plates over the range 0.02-2 mg/ml. 100 μ l of diluted solutions were pipetted in each well containing 90 μ l broth. 10 μ l of working inoculum suspension (2×10^4 CFU/ml) was added to the well. A number of wells were reserved in each plate for control of sterility (no inoculum added), inoculum viability (no test compound added), and DMSO inhibitory effect. The inoculated plates were then incubated for 37°C for 24 h. The minimal inhibitory concentration (MIC) was detected as the lowest concentration of the test compound in plate at which no visible growth of microorganism found. The bacterial growth was indicated by the turbidity. All tests were performed in triplicate for each microorganism tested.

Insect species

Adults of *Tribolium castaneum* were reared on wheat flour and adults of *Callosobruchus maculatus* were reared on cowpea seeds at $25 \pm 1^\circ\text{C}$ and $65\% \pm 5\%$ in laboratory condition. Adult insects of mixed sex, 7-14 days old, were used for bioassay test.

Repellent bioassay

Repellency assay of the metal complexes were carried out according to the methods described by Jilani and Saxena, 1990²⁷ with necessary modification at $25 \pm 1^\circ\text{C}$ and $65\% \pm 5\%$ relative humidity (RH). Half of the Whatman filter paper disc (diameter 9 cm) was prepared by dissolving 0.5 mg, 2 mg and 5 mg of ligand and its metal complexes in 1 ml acetone. Each solution was applied to half a filter paper disc uniformly with a micropipette. The other half of the filter paper was treated only with acetone and treated as control. The treated and control half disc were allowed to be air dried so that the solvent evaporated completely. Each treated and untreated halves were attached edge to edge with adhesive tape and placed in petridishes. 20 adult (7 days old) beetles of either sex were released at the center of each filter paper disc. The dishes were then covered with net and sealed properly so that insects get sufficient air for survival and could not escape from the petridishes. Insects that settled on each half of the filter paper discs were counted after 4hrs.

Percentage repellency (PR)

Numbers of *C. maculatus* and *T. castaneum* present on the treated and untreated portions of the filter paper halves were recorded after exposure. Percentage repellency was calculated as described by²⁸ as follows:

$$\text{PR} = \left[\frac{N_c - N_t}{(N_c + N_t)} \right] \times 100$$

where,

N_c - number of insects on the untreated area after the exposure interval

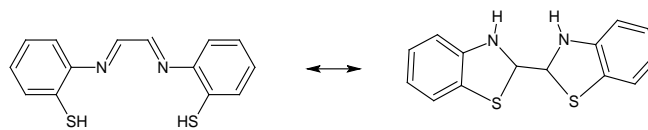
N_t - the number of insects on the treated area after the exposure interval. The mean number of insects on the treated portion of the filter paper was compared with the number on the untreated portion from three replicas of the experiment. Results were presented as the mean of percentage repellency \pm the standard error.

RESULT AND DISCUSSION

IR spectra

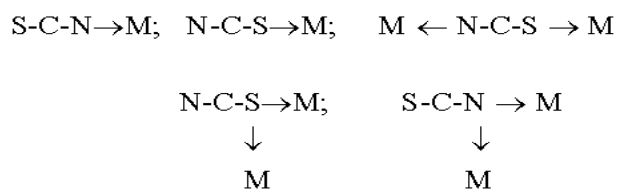
IR spectroscopy have proven to be the most efficient technique to give enough information to illustrate the way of bonding of the ligands to the metal ions, particularly in the absence of a commanding technique such as X-ray crystallography. In order to study the binding mode of the Schiff base to the metal ion in the complexes, the IR spectrum of the free Schiff base (Fig 1A) was compared with the spectra of the transition metal complexes (Fig 1B and C). These peaks change either in their positions and/or their intensities upon chelation. In the IR spectra of ligand (Fig 1A), the absence of ν SH absorption band in the region $2600\text{-}2550\text{ cm}^{-1}$ and appearance of a strong and sharp ν (NH) and δ (NH) at 3375 cm^{-1} and 1676 cm^{-1} respectively in the ligands is a strong evidence for the existence of benzothiazoline structure of these ligands²⁹ and not the Schiff base structure.

In the spectra of metal complexes, band due to N-H vibration disappear, indicating the chelation of nitrogen with the metal ion, and a new band at 1600 cm^{-1} is observed, which can be assigned to ν (C=N). This band suggests that in the presence of metal ion, the benzothiazoline ring rearranges (Scheme 1) to give the Schiff Base which finally acts as the tri- or tetradentate ligand.



Scheme 1. Rearrangement of benzothiazoline ring

Presence of thiocyanate, for which strong absorptions in the $2110\text{-}2075\text{ cm}^{-1}$ region remain isolated, is confirmed by infrared spectroscopy. As thiocyanate is a heteroatomic ambidentate ligand³⁰⁻³³ it shows different molecular architectures through its versatile ligational modes (Scheme 2). The spectra of Zn and Ni complexes exhibit a very strong and sharp absorption band in the region of ($2075\text{ to }2100\text{ cm}^{-1}$) (Fig.1B and C) corresponding to the asymmetric stretching vibrations of the terminal N- bonded



Scheme 2. Different ligational motifs of thiocyanate

Table 2. Disc diffusion study showing the inhibition zone diameter (mm) of metal complexes (1 and 2) and the ligand against bacterial and fungal strain. Results are mean \pm S.E of triplicate experiments.

Compound	Gram-negative bacteria		Gram-positive bacteria		Fungus	
	<i>K. pneumoniae</i>	<i>P. mirabilis</i>	<i>S. aureus</i>	<i>B. subtilis</i>	<i>C. albicans</i>	<i>A. niger</i>
Ligand (H ₂ L)	06 \pm 0.87	08 \pm 0.41	08 \pm 0.65	08 \pm 0.35	06 \pm 0.90	06 \pm 0.54
[Zn(HL)(NCS)]	10 \pm 0.83	08 \pm 1.20	12 \pm 0.38	14 \pm 0.59	11 \pm 0.86	15 \pm 0.65
[Ni(H ₂ L)(NCS) ₂]	13 \pm 0.44	12 \pm 0.30	19 \pm 1.10	20 \pm 0.96	12 \pm 0.60	16 \pm 0.51
Gentamicin	25 \pm 0.02	22 \pm 0.09	23 \pm 0.02	33 \pm 0.04	-	-
Fluconazole	-	-	-	-	34 \pm 0.00	30 \pm 0.00

Compounds 2 showed strongest antimicrobial activity against all microbial strain studied than compound 1. It is very clear from the inhibition zone values that both the compounds showed stronger activity against Gram positive in comparison to Gram negative bacteria and fungus.

The results of MIC values (Table 3) indicated that new metal complexes inhibited all bacterial microorganism tested. The MIC values assessed by broth microdilution method support the results obtained from Agar disc diffusion method (Table 2). The Gram positive bacteria were more sensitive to the Ni complexes. Lower MIC value indicates more toxic the compound and higher MIC value indicates less toxicity of the compound. Thus the MIC values and IZD (inhibition zone diameter) values indicate Ni complexes were more toxic towards Gram positive strains than Gram negative strains. The stronger activity of metal complexes against the Gram positive bacteria can be explained by the difference in the cell wall structure.⁴² The walls of the Gram negative cells are more complex and multilayered than those of Gram positive cells because of relatively high lipid content in addition to protein and mucopeptide. It is suggested that the antimicrobial activity of the complexes is due to either by killing the microbes or inhibiting their multiplication by blocking their active sites.⁴³

The comparison of antimicrobial activity of the free ligand and its complexes indicates that complexation with metals has a synergistic effect on the antimicrobial activity

Table 3. MIC value (μ g/mL) of metal complexes (1 & 2) for different microorganism tested.

Compounds	<i>K. pneumoniae</i>	<i>P. mirabilis</i>	<i>S. aureus</i>	<i>B. subtilis</i>
[Zn(HL)(NCS)]	< 1.0	< 1.0	> 0.6	> 0.8
[Ni(H ₂ L)(NCS) ₂]	< 1.0	> 0.8	< 0.4	< 0.6
Gentamicin	< 0.15	< 0.15	0.07	0.06

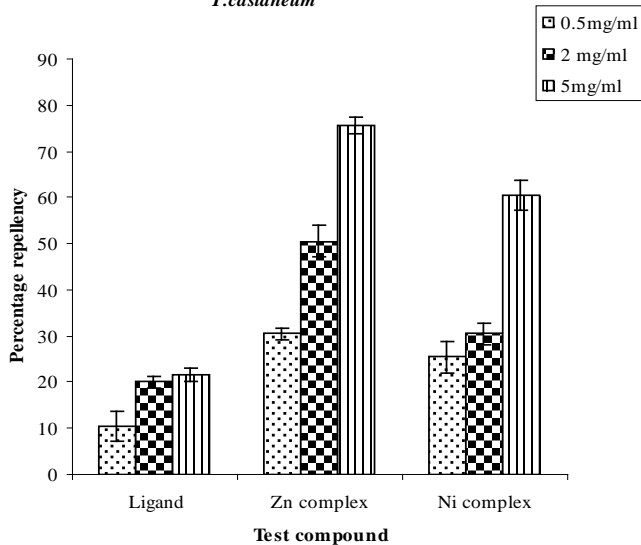
of these compounds and the antimicrobial activity depends upon the type of metal ion present.¹⁹ The possible reason of higher antimicrobial activity shown by the newly synthesized compounds than its parent ligand can be explained by chelation theory.⁴⁴ In chelated complex the positive charge of the metal is partially shared with donor

groups of the ligands and there is an electron delocalization over the whole chelated ring^{44,45}. Thus chelation considerably reduces the polarity of the metal ion thereby enhancing its lipophilic character which subsequently favors its permeation through the lipid layer of the bacterial membrane.^{46,47} Further, it has also been suggested that some functional groups such as azomethine (-C=N-) present in these compounds play an important role in antibacterial and antifungal activity.^{48,49} Thus the presence of azomethine groups may play a dominating role in enhancement of the hydrophobic and liposolubility character of the overall molecules. However, in Gram negative bacteria an unusual lipid, lipopolysaccharide (LPS) in the outer membrane (outside the peptidoglycan layer) serves as an effective barrier against lipophilic molecules and thus slower the penetration rate of the hydrophobic molecules⁵⁰. The greater susceptibility of the Gram positive bacteria toward metal complexes in comparison to Gram negative bacteria may be due to the lack of LPS in their outer membrane.

It has been reported that chelated complex deactivate various cellular enzymes, which play a vital role in various metabolic pathways of these microorganism⁴⁴ which may ultimately affect the replication of DNA and thus caused inhibition of bacterial growth. The role of other properties such as solubility, conductivity, dipole moment of the compound may be affected by the presence of metal ions, which may also be possible reason for increasing the biological activity of the metal complex as compared to the parent ligand from which they derived.⁴⁴

From the in vitro antimicrobial assay, all the novel compounds are found to possess moderate to high antimicrobial properties. However, bioactivities of synthesized metal complexes are lower than those of the tested commercial antibiotics at similar concentrations. These results suggest that antibacterial activities of the ligand increased after coordination with metal ions. These observations are similar to the bioactivities of those previously reported Zn (II), Ni (II) Schiff-base complexes.^{20,51}

Percentage repellency of Ligand and metal complex against *T. castaneum*



Percentage repellency of ligand and metal complex against *C. maculatus*

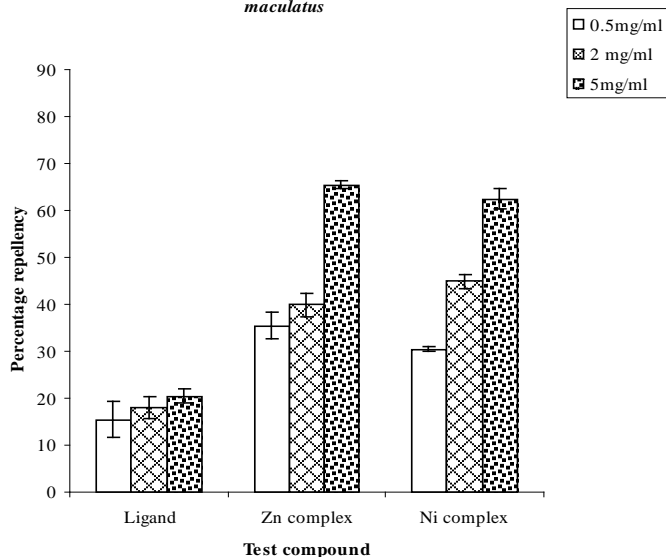


Figure 3. Bar diagram representing the percent repellency of the ligand and metal complexes (1 & 2) at different concentration to (A) *T. castaneum* and (B) *C. maculatus*

Insect repellent activity

The repellent action of ligand and metal complexes were studied against *T. castaneum* and *C. maculatus* and percent repellency of the ligand and complexes are represented in the Figure 3. Low repellent activity of both complexes was found even at 0.5mg/ml concentration. Repellent action was highly dependent upon the concentration of the compound. The maximum activity (70.5%) was observed at the highest concentration (5mg/ml) of exposure for Zn complex against *T. castaneum* adults. Zn complex had strong repellent action against both insect species in comparison to the Ni complex. Free ligand had weak repellent activity against both the insect. Briefly, it can be concluded that the effect of Zn complex was evident against both the insect species at the highest concentration after the exposure period. Insecticidal activity of Schiffbase derived from thiadiazole derivatives

with salicylaldehyde and their metal complex with Mo(IV) has been reported against bollworm infestation of mung bean.¹²

CONCLUSION

In the present study, the synthesis and characterization of tetradentate Schiff base complexes with two transition metals involving Zn(II) and Ni(II) are described. The *in vitro* antibacterial and antifungal activities of the synthesized complexes had been studied by testing them in four bacterial strain and two fungal strain which showed considerable inhibitory effect as compared with the standard antibiotics and antifungal agent. Newly synthesized nickel complex exhibited highest antimicrobial activities. The fungus species were less susceptible to the metal complexes than bacterial strain studied. It has been suggested that the bioactivity of ligand increased upon coordination due to chelation which ultimately increase the lipophilic nature of metal and, thereby, facilitating rapid penetration through microbial cell wall⁴⁶. However, presence of lipopolysaccharide in the outer membrane of Gram negative bacteria affects the penetration rates of lipophilic molecules⁵⁰. As a result, lipophilic metal complexes may show reduced activity (smaller inhibition zone diameter and higher MIC value) in Gram negative bacteria than Gram positive bacterial strain as found in the present study in both zinc and nickel complexes. The repellent activity against the stored grain pest shown by the Zn complex also established the potentiality of this complex as pesticidal agent. Zn complex of the Schiffbase ligand may be applied to control the stored grain pest with further modification. Therefore, from the present study it can be concluded that both the novel compounds possess moderate to high antimicrobial properties and the Zn complexes may be used as potential pesticides in the integrated pest management with further modification.

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REFERENCES

- P.G. Cozzi. Metal-Salen Schiff base complexes in catalysis: practical aspects. *Chem Soc Rev.* **2004**, 33(7), 410-421.
- S.R. Collinson, D.E. Fenton. Metal complexes of bibrachial Schiff base macrocycles. *Coord Chem Rev.* **1996**, 148, 19-40.
- S. Kumar, D.N. Dhar, P.N. Saxena. Application of metal complexes of Schiff bases: A review. *J Scientific Indust Research.* **2009**, (68), 181-187.
- H.F. Abd El-Halim, M.M. Omar, G.G. Mohamed. Synthesis, structural, thermal studies and biological activity of a tridentate Schiff base ligand and their transition metal complexes. *Spectrochim Acta A Mol Biomol Spectrosc.* **2011**, 78(1), 36-44.
- T.B. Ravooof, K.A. Crouse, M.I.M. Tahir, F.N. How, R. Rosli, D.J. Watkins. Synthesis, characterization and biological activities of 3-methylbenzyl 2-(6-methyl pyridin-2-ylmethylene) hydrazine carbodithioate and its transition metal complexes. *Transition Met Chem.* **2010**, 35(7), 871-876.
- N.P. Priya, S. Arunachalam, A. Manimaran, D. Muthupriya, C. Jayabalakrishnan. Mononuclear Ru (III) Schiff base complexes: Synthesis, spectral, redox, catalytic and biological activity

- studies. *Spectrochim Acta A Mol Biomol Spectrosc.* **2009**, 72(3), 670-676.
7. S. Mandal, A.K. Rout, A. Ghosh, G. Pilet, D. Bandyopadhyay. Synthesis, structure and antibacterial activity of manganese (III) complexes of a Schiff base derived from furfurylamine. *Polyhedron*, **2009**, 28 (17), 3858-3862
 8. S. Mandal, T.K. Karmakar, A. Ghosh, M. Fleck, and D. Bandyopadhyay, Synthesis, crystal structure and antibacterial activity of a group of mononuclear manganese (II) Schiff base complexes. *Polyhedron*, **2011**, 30, 790-795.
 9. N. Raman, V. Muthuraj, S. Ravichandran and A. Kulandaisamy, "Synthesis, characterisation and electrochemical behaviour of Cu(II), Co(II), Ni(II) and Zn(II) complexes derived from acetylacetone and p-anisidine and their antimicrobial activity", *Proceedings of Indian Academy of Science (Chem. Sci.)*, **2003**, 115(3), 161-167.
 10. S.E. Etaiw, D.M.A. El-Aziz, E.H. Abd El-Zaher, E.A. Ali, "Synthesis, Spectral, antimicrobial and antitumor assessment of Schiff base derived from 2-aminobenzothiazole and its transitional metal complexes", *Spectrochimica Acta A: Molecular and Biomolecular Spectroscopy*, **2011**, 79, 1331-1337.
 11. N. Raman, J. Joseph, S. Muthu Kumar, S. Sujatha, and K. Sahayaraj. Insecticidal activity of the schiff - base derived from anthranilic acid and acetoacetanilide and its copper complex on Spodopteralitura (Fab.) *J Biopesticides*. **2008**, 1(2), 206- 209.
 12. L. Zhu, N. Chen, H. Li, F. Song, and X. Zhu. Synthesis, Characterization and biological activities of Schiff bases of 2-amino-5 mercapto-1,3,4-thiadiazole and their Mo(VI) complexes. *Huazhong Shifan Daxue Xuebao Ziranxueban*, **2003**, 37,499-502.
 13. S.E. Castillo-Blum, N. Barba-Behrens. Coordination chemistry of some biologically active ligands. *Coord Chem Rev.* **2000**, 196(1): 3-30.
 14. S. Kita, H. Furutachi, H. Okawa. (μ -Phenoxo) $2\text{CoII}(\text{M})$ (M= Mn, Co, Zn) Complexes with a Co (salen) Entity in a Macrocyclic Framework: Core Structures and Neighboring MII Effects upon Oxygenation at the Co (salen) Center. *Inorg Chem*, **1999**, 38(18), 4038-4045.
 15. O. Atakol, H. Nazir, C. Arici, S. Durmus, I. Svoboda, H. Fuess. Some new Ni, Zn heterodinuclear complexes: square-pyramidal nickel (II) coordination. *Inorg Chim Acta*. **2003**, 342, 295-300.
 16. Y.L Sang, X.S. LIN. Syntheses and crystal structures of two Schiff-base copper (II) complexes with antibacterial activities. *J Coord Chem*, **2010**, 63(2), 315-322.
 17. R.M. Issa, S.A. Azim, A.M. Khedr, D.F. Draz. Synthesis, characterization, thermal, and antimicrobial studies of binuclear metal complexes of sulfa-guanidine Schiff bases. *J Coord Chem*. **2009**, 62(11), 1859-1870.
 18. Y. Xiong. Synthesis, Characterization, and Antibacterial Activity of Nickel (II) Complexes With Schiff Bases. *Synth React Inorg Met-Org Nano-Met Chem*. **2013**, 43(8), 961-965.
 19. M.X. Li, L.Z Zhang, C.L. Chen, J.Y. Niu, B.S Ji.. Synthesis, crystal structures and biological evaluation of Cu(II), and Zn(II) complexes of 2-benzoylpyridine Schiff bases derived from S-methyl and S-phenylthiocarbazates. *J Inorg Biochem*, **2012**, 106, 117-125.
 20. Z.H. Chohan, H. A. Shad, M.H. Youssoufi, T.B. Hadda, Some new biologically active metal based sulfonamide. *E J Med Chem*. **2010**, 45, 2893-2901.
 21. N. Ahmed, M. Riaz, A. Ahmed, and M. Bhagat. Synthesis, Characterisation, and Biological Evaluation of Zn(II) Complex with Tridentate (NNO Donor) Schiff Base Ligand. *Inter J. Inorg. Chem*. **2015**, ID 607178
 22. M. Ahmed Abu-Dief and Ibrahim M.A. Mohamed. A review on versatile applications of transition metal complexes incorporating Schiff bases. *Beni-suef university journal of basic and applied sciences*. **2015**, 4 (2015) 119 e133.
 23. S.N. Kotkar and H. D. Juneja. Synthesis, Characterization, and Antimicrobial Studies of N, O Donor Schiff Base Polymeric Complexes. *Journal of Chemistry*. **2013**, 479343.
 24. A.W. Bauer, W.M.M. Kirby, J.C.T. Sherris, M. Turck. Antibiotic susceptibility testing by a standardized single disk method. *Am J Clin Pathol*. **1966**, 45(4), 493.
 25. National Committee for Clinical Laboratory Standards (NCCLS). Proceedings of the ninth international supplement on performance standards for antimicrobial susceptibility test. M100-S9, Wayne PA, **1999**.
 26. I.H.N. Bassole, A.S. Quattara, R. Nebie, C.A.T. Quattara, Z.I. Kabore, S.A. Traore. Chemical composition and antibacterial activities of the essential oils of Lippiachevalieri and Lippia multi-flora from Burkina Faso. *Phytochem*. **2003**, 62, 209-212.
 27. G. Jilani, R.C. Saxena. Repellent and feeding deterrent effects of turmeric oil, sweetflag oil, neem oil, and a neem based insecticide against lesser grain borer (Coleoptera, Bostrychidae). *J Econom Entomol*. **1990**, 83, 629-634.
 28. L. Nerio, J. Oliver-Verbel, E. Stashenko. Repellency activity of essential oils from seven aromatic plants grown in Colombia against *Sitophilus zeamais* Motschulsky (Coleoptera). *J stored Pro Res*. **2009**, 45, 212-214.
 29. R.K. Sharma, R.V. Singh, J.P. Tandon, Zr (IV) complexes of some sulphur donor ligands. *J Inorg Nucl Chem*. **1980**, 42(9), 1267-1270.
 30. H. Deng, Y.C. Qiu, Y.H. Li, Z.H. Liu, R.H. Zeng, M., Zeller, S.R. Batten. Reversible shrinkage and expansion of a blue photofluorescent cadmium coordination polymer and in situ tetrazole ligand synthesis. *Chem Commun*. **2008**, (19), 2239-2241.
 31. D.A. Buckingham. The linkage isomerism of thiocyanate bonded to cobalt (III). *Coord Chem Rev*, **1994**, 135, 587-621.
 32. M. Dakovic, Z. Popovic, G. Giester, M. Rajic-Linarcic. Thiocyanate complexes of the group 12 metals with pyridine-2-carboxamide: Synthesis and structural characterization. *Polyhedron*, **2008**, 27(1), 210-222.
 33. Y. Bai, W.L. Shang, D.B. Dang, H. Gao, X.F. Niu, Y.F. Guan. Synthesis, crystal structure and luminescent properties of a thiocyanato bridged two-dimensional heteronuclear polymeric complex of Cadmium (II) and Copper (II). *Inorg Chem Commun*. **2008**, 11(12), 1470-1473.
 34. M. Dakovic, Z. Popovic, G. Giester, M. Rajic-Linarcic. Synthesis, spectroscopic and structural investigation of $\text{Zn}(\text{NCS})_2(\text{nicotinamide})_2$ and $[\text{Hg}(\text{SCN})_2(\text{nicotinamide})]_n$ *Polyhedron*. **2008a**, 27(1), 465-472.
 35. S. Satapathi, S. Das, K. Bhar, R.K. Kumar, T.K. Maji, B.K. Ghosh. Syntheses, structures and luminescence behaviors of mono- and dinuclear complexes of type $[\text{M}(\text{L})(\text{NCS})_2]_n$ [$\text{M} = \text{Zn}/\text{Hg}$, $n = 1$; $\text{M} = \text{Cd}$, $n = 2$; $\text{L} = (\text{N}, \text{N}$ -diethyl, N' -(pyridin-2-yl)benzylidene)ethane-1,2-diamine]: variation of coordination matrices and nuclearities with the change of congeneric metal ions. *Polyhedron*. **2011**, 30 (2), 387-396.
 36. K. Nakamoto. Infrared and Raman Spectra of Inorganic and Coordination Compounds. In 'Handbook of vibration spectroscopy'. Wiley, New York ISBN: 9780470027325, **2006**
 37. A.A. Soliman, W. Linert. Investigations on new transition metal chelates of the 3-methoxy-salicylidene-2-aminothiophenol Schiff base. *Thermochim Acta*. **1999**, 338 (1), 67-75.
 38. S. Priyarega, D. Senthil Raja, S. Ganesh Babu, R. Karvembu, T. Hashimoto, A. Endo, K. Natarajan, Novel binuclear palladium (II) complexes of 2-oxoquinoline-3-carbaldehyde Schiff bases: Synthesis, structure and catalytic applications. *Polyhedron*. **2012**, 34(1), 143-148.
 39. M. Tamizha, K. MuthuMereiter, K. Kirchner, R. Karvembu. Ruthenium (II) carbonyl complexes containing 'pincer like' ONS donor Schiff base and triphenylphosphine as catalyst for selective oxidation of alcohols at room temperature. *J Organomet Chem*. **2012**, 700, 194-201.
 40. K. Nakamoto. Infrared and Raman spectra of coordination compounds. Wiley, New York, **1997**.
 41. A.K. Sharma, S. Chandra. Complexation of nitrogen and sulphur donor Schiff's base ligand to Cr (III) and Ni (II) metal ions: Synthesis, spectroscopic and antipathogenic studies. *Spectrochim Acta A Mol Biomol Spectrosc*. **2011**, 78(1), 337-342.
 42. R.V. Singh, P. Chaudhary, S. Chauhan, M. Swami. Microwave-assisted synthesis, characterization and biological activities of organotin (IV) complexes with some thio Schiff bases. *Spectrochim Acta A Mol Biomol Spectrosc*. **2009**, 72(2), 260-268.

43. M. Nath, S. Pokharia, X.Song, G. Eng, M. Gielen, M. Kemmer, M. Biesemans, R. Willem, D. De Vos. New organotin (IV) derivatives of dipeptides as models for metal–protein interactions: in vitro anti-tumour activity. *Appl Organomet Chem.* **2003**, 17(5), 305-314.
44. A.A. Adel Emará. Structural, spectral and biological studies of binuclear tetradentate metal complexes of N₃O Schiff base ligand synthesized from 4,6-diacetylresorcinol and diethylenetriamine. *Spectrochim Acta A Mol Biomol Spectrosc.* **2010**, 77, 117-125.
45. R.S. Srivastava. Pseudotetrahedral Co (II), Ni (II) and Cu (II) complexes of N¹-(O-chlorophenyl)-2-(2', 4'-dihydroxyphenyl)-2-benzylazomethine their fungicidal and herbicidal activity. *Inorg Chim Acta.* **1981**, 56, 65-67.
46. Z.H. Chohan, C.T. Supuran, A. Scozzafava. Metal binding and antibacterial activity of ciprofloxacin complexes. *J Enz Inhibit Med Chem.* **2005**, 20(3), 303-307.
47. S.U. Rehman, Z.H. Chohan, F. Gulnaz, C.T. Supuran. In-vitro antibacterial, antifungal and cytotoxic activities of some coumarins and their metal complexes. *J Enzyme Inhib Med Chem.* **2005**, 20(4), 333-340.
48. Z.H. Chohan, A.U. Shaikh, A. Rauf, C.T. Supuran. Antibacterial, antifungal and cytotoxic properties of novel N-substituted sulfonamides from 4-hydroxycoumarin. *J Enzyme Inhib Med Chem.* **2006**, 21(6), 741-748.
49. Z.H. Chohan, H.A. Shad, F.U.H. Nasim. Synthesis, characterization and biological properties of sulfonamide-derived compounds and their transition metal complexes. *Appl Organomet Chem.* **2009**, 23(8), 319-328.
50. G.N. Cohen. The outer membrane of Gram-negative bacteria and the cytoplasmic membrane Chapter 2 In "Microbial Biochemistry". pp. 558 Springer ISBN 978-90-481-9436-0, **2011**.
51. B.K. Singh, A. Prakash, H.K. Rajour, N. Bhojak, D. Adhikari.. Spectroscopic characterization and biological activity of Zn(II), Cd (II), Sn (II), and Pb(II) complexes with Schiff base derived from pyrrole-2-carboxaldehyde and 2- aminophenol. *Spectrochim Acta A Mol Biomol Spectrosc.* **2010**, 76, 376-383.