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Synthesis, characterization and biological evaluation of heterocyclic triazole derived Schiff base ligands comprising Mn(II) complexes: Implications of their DNA/protein binding docking and anticancer activity studies

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Schiff base ligands comprising heterocyclic moieties deserve distinct consideration because of their excellent chemotherapeutic and antioxidant properties as biologically active agents. In present investigation, two novel heterocyclic triazole derived Schiff base ligands have been synthesized using 3-chlorobenzaldehyde (L1), 4-methoxybenzaldehyde (L2) with 1H-1,2,4-triazol-3-amine backbone that are biologically active. Mn(II) complexes have been synthesized by combing ligands in 1:2 molar ratio (metal:ligand), their structure and bonding nature are recognised by respective physical, spectral and analytical data. The ligands (L1 & L2) and their metal complexes are characterized by elemental analyses, electronic, FT-IR, ^{1}H and ^{13}C NMR and EPR spectroscopy techinques. Antimicrobial activity of the synthesized L1, L2 and their metal complexes are tested against *Bacillus subtilis* (Gram-positive, catalase-positive bacterium) as well as Fungi namely *Phylium Aphanidematum, Macrophomina phasiolina, Fusarium oxysporum*. Both the ligands and metal complexes exhibit excellent antimicrobial activity under low inhibitory concentration such MIC $\leq$ 250 µg/mL. Upon co-ordination, antimicrobial properties have been enhanced by 21%. The anticancer activity of the synthesized complex has been investigated against human tumour cell lines (Breast cancer MCF-7 cells) demonstrated that L1M complex displays potent inhibition against MCF-7. Using this molecular docking study, we can predict the complex–biomolecular interaction and it plays vital role in the drug discovery and also it is a step by step process which is used to place synthesised compounds into the binding sites of the DNA molecule. Further, Molecular DNA docking results demonstrated encouraging responses, thereby opening up new avenues for the application of the synthesized inorganic triazole derivative complexes as leads for the development of novel anti-cancer drugs.

Keywords: Heterocyclic Schiff base, 1H-1,2,4-triazol-3-amine ligands, Mn(II) complexes, Inorganic complex**,** Antimicrobial studies, Molecular docking

Triazoles and their derivatives have attracted immensely specific research interest in modern heterocyclic chemistry in the view of their substantial pharmacological and biological activities[1]. In particular, 1,2,4-triazole derived Schiff base ligands regulate the growth of many harmful micro-organisms and possess excellent antibacterial, antiviral, antioxidant and anti-inflammatory properties, hence appropriate to be used as biocides[2-4]. According to the World Health Organisation report millions of peoples were died due to the infections caused by the micro-organisms like fungi, virus, bacteria etc.[5]. The antibiotics must be less toxic for healthy cells and must have maximum efficiency towards killing the micro organisms[6–8]. In the recent years, there are some restricted antibiotics which can cause the failure in the antimicrobial therapy and also the rate of curing capability is also high with maximum cost[9–16]. Usually, Gram-positive bacteria specialized in the extrusion of different doubted substance in the out of the cell wall (efflux bomb); the limited access of the antimicrobial agents to its miserable site of exchange is always active one. So, it should be a good antibiotic drug[17]. The antibiotics having metal complexes are more active towards the microbial studies. Specifically transition metal complexes, having low molecular weight can be used to response for the probable structural property and also it has more potential activity towards the microorganisms[18–20]. Manganese complexes are easily binds with protein and form metal-protein complexes and also exhibits great biological active results. These types of complexes easily exchange the electrons and store the ions which creates the enormous interests in

synthesise of manganese containing complexes with low molecular weight[21]. Also, manganese derivatives have been reported to be used for environmental, industrial and agricultural applications. Not only has an upsurge of importance taken place in experimental studies, but there has also been a repeated concern in the structural elucidation of manganese complexes.

Several Schiff bases are reported to possess remarkable antibacterial, antifungal, and anticancer activities[22]. In such class of compounds, the C=N moiety is important for biological activity. Abdel-Rahman *et al.*[22] have reported number of transition metal complexes by using variety of Schiff base ligands and have studied their different biological activities such as antimicrobial, anticancer, antifungal, etc. Triazole derived Schiff base ligand Mn(II) complex 2-[(1*Z*)-*N*-(1*H*-1,2,4-triazol-3-yl)-etanimidoyl]phenol was synthesized by condensation of 3-amino-1,2,4-triazole with 2-hydroxyacetophenone and demonstrated as an efficient antibacterial agent against several bacterial strains: *Escherichia coli, Salmonella typhi, Bacillus subtilis, Klebsiella pneumonia,* and *Staphylococcus aureus by* Summara *et al*[23]. The synthesis and characterization of divalent transition metal complexes e.g., Co(II), Cu(II), Cd(II) and Mn(II) with nicotinohydrazide ligand was reported by Shen *et al.*[24]. The complex also used for in vitro cell experiment to test the antitumour effect. The results revealed that the uncomplexed ligand show cytotoxic effect than the metal complexes. Metal complexes can effectively decrease the proliferation rate of different type of cancerous cell line like human gastric cancer cells, human esophageal cancer cell line (ECA109). Anticancer activity of the synthesized Mn(III), Zn(II) and Pt(II) macroacyclic complexes against human gastric (AGS, IBRC C 10071) and lung (A549; IBRC C10080) cell lines.[25] Ispir *et al.*[26] described the Schiff bases of 2,6-diacetylpyridine and 2-pyridine carboxaldehyde with 4-amino-2,3-dimethyl-1-phenyl-3-pyrozolin-5-one[4,4′-(1E,1′E)-(1,1′-(pyridine-2,6-diyl)bis(ethan-1-yl-1-ylidene))bis(azan-1-yl-1-ylidene)bis(1,5-dimethyl-2-phenyl-1H-pyrazol-3(2H) one), and (E)-1,5-dimethyl-2-phenyl-4-(1-(pyridin-2-yl)ethylideneamino)-1H-pyrazol-3(2H)-one] and their Co(II), Cu(II), Ni(II), Mn(II) and Cr(III) complexes exhibit antibacterial and antifungal activities against *E. coli, Staphylococcus aureus, Klebsiella pneumoniae, Mycobacterium smegmatis, P. aeruginosa, Enterobacter cloacae,* and *Micrococcus leteus*[26]. Four new Mn(III) Schiff base complexes were synthesized and characterized. The complexes have general formula [MnClL^x] in which L represents a Schiff base ligand derived from condensation of *meso*-1,2-diphenyl-1,2-ethylenediamine with salicylaldehyde or its 3-OMe-, 5-Br-, or 5-OMe-derivatives (x = 1–4, respectively). The crystal structure of [MnClL^1] was characterized by X-ray crystallography. The in vitro anticancer activity of these complexes was evaluated by MTT and apoptosis assays against human breast (MCF-7) and liver (Hep G2) cancer cells. The complexes exhibited considerable antiproliferative activity against both cell lines (IC_{50} = 10.8–21.02 μM). Docking simulations using AUTODOCK were also carried out. The results showed that all complexes fitted into the minor groove region of DNA[27].

In the light of the foregoing, this work aimed to prepare two new class of triazole derived Schiff base ligands using benzene derivatives of 3-chlorobenzaldehyde (L1), 4-methoxybenzaldehyde (L2) with 1H-1,2,4-triazol-3-amine. The Schiff base ligand act as bidentate and coordinate with manganese in the ratio of 2:1 (ligand:metal). These ligands can form 3-member chelating ring. In the present studies, manganese has been focussed due to their smaller size and comparatively higher nuclear charge.

The synthesised metal complexes treated with the gram positive *Bacillus subtilis* and gives efficient activity. Anticancer cell line testing with MCF 7 studies indicated that these complexes arrested the cell cycle efficiently and promoted tumour cell destruction *via* a reactive oxygen species (ROS)-mediated mitochondrial pathway.

Materials and Methods

The chemicals 3-chlorobenzaldehyde, 4-methoxybenzaldehyde, 1H-1,2,4-triazol-3-amine, Manganese chloride were purchased from Sigma-Aldrich and used without further purification. The solvents were purchased from the Merck used after purification using suitable distillation procedures.

Physical measurements

Elemental analyses (C, H, N and S) were carried out using elemental various EL III CHNOS elemental analyser. Fourier transform infrared (FT-IR) spectra the compounds were recorded using Shimadzu 8400S FT-IR spectrophotometer in the range of 4000-400 cm^{-1} using KBr pellets. Electronic spectra were recorded using Shimadzu UV-2450 spectrophotometer. The X-band of electron paramagnetic resonance (EPR) spectra of Mn(II) complexes in the acetonitrile were recorded at the

room temperature, tetracyanoetylene as the g (2.0027) marker. ^{1}H and ^{13}C NMR spectrums were recorded for ligands (L1 & L2) on Varian XL-200 NMR instrument using deuterated DMSO solvent.

Molecular docking studies

Molecular docking is one of the clear theoretical study for determining the binding energy of our synthesised compounds with biomolecules like DNA and proteins. The molecular structures of the Mn(II) complexes converted into moles files using mercury V3.6. The mol files of the synthesised Mn(II) complexes were optimized using Gaussian 09 computational suite with the basis set of LanL2DZ. The crystal structures of DNA hexamer d(CGATCG)2 (PDB ID: 1Z3F) was downloaded from protein data bank (http://www.rcsb.org/pdb) in PDB format. Discovery studio software was used to delete the ligand and water molecule already present in the biomolecules. The docking studies for L1 and L2 were carried out using Autodock vina program and the complexes were prepared using Autodock tools 1.5.6. The grid map value was set to be 120 × 120 × 120 Å for xyz axis grid spacing value of 0.680 Å for DNA.

Synthesis of the compounds

Synthesis of (E)-N-(2-chlorobenzylidene)-1H-1,2,4-triazol-3-amine (L1)

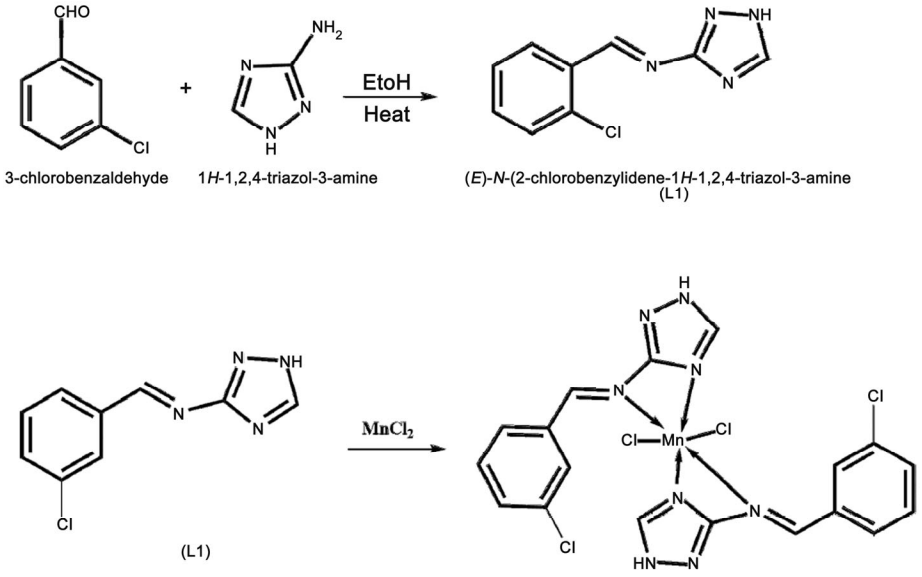
A mixture of M-chlorobenzaldehyde (1 mmol) and 3-amino-1,2,4-triazole (1 mmol) was dissolved in 10 mL of ethanol which was continuously stirred and refluxed for 4 h in an oil bath at 60 ºC. The compound was then allowed to evaporate at the room temperature. The yellow coloured product obtained was washed with diethyl ether and chloroform. Then the yellow solid was recrystallized using ethanol. Purity of the compound was checked by thin layer chromatography. Chemical formula: $C_9H_7ClN_4$; elemental analysis (%): C, 52.31; H, 3.41; Cl, 17.16; N, 27.11; IR (KBr pellets, υ, cm^{-1}): 1650 (C=N), 1340 (Ar-H), 1596 (N-H); UV-visible absorption [(λ_{max}, nm), solvent, acetonitrile: chloroform (1:1) mixture]: 375, 328, 272 and 218.

Synthesis of L1M metal complex

In the preparation of Mn(II) complex, 5 mL ethanolic solution of L1 and manganese chloride were mixed with 2:1 ratio at 70 ºC using oil bath. The content was then kept for evaporation. The sandal coloured solid metal complex obtained was washed with ethanol and water. The ligand L1 and metal complex L1M were synthesized as given in Scheme 1. Chemical formula: $C_{18}H_{14}C_{l4}MnN_8$; elemental analysis (%): C, 40.10; H, 2.62; N, 20.79; IR (KBr pellets, υ, cm^{-1}): 1642 (C=N), 1345 (Ar-H), 1573 (N-H); UV-visible absorption [(λ_{max}, nm), solvent, DMSO]: 573, 460, 315 and 228.

Synthesis of (E)-N-(4-methoxybenzylidene)-1H-1,2,4-triazol-3-amine (L2)

Anisaldehyde (1 mmol) and 3-amino-1,2,4-triazole (1 mmol) were dissolved in 10 mL of acetonitrile:ethanol mixture (1:1) which was continuously stirred for 15 h at room temperature. The



Scheme 1 — Reaction pathway for L1 and L1M complexes

compound was then allowed to evaporate in the dedicator for 48 h. The light yellow coloured product obtained and washed cold ethanol. Chemical formula: $C_{10}H_{10}N_4O$; elemental analysis (%): C, 59.40; H, 4.98; N, 27.71; O, 7.91; IR (KBr pellets, υ, cm^{-1}): 1608 (C=N), 1358 (Ar-H), 1583 (N-H); UV-visible absorption [(λ_{max}, nm), solvent, acetonitrile:chloroform (1:1)]: 370, 322, 265 and 217.

Synthesis of L2M metal complex

For the synthesis of L2M complex, manganese chloride was dissolved in 2 mL of water and added dropwise in 5 mL ethanolic solution of L2 and the mixture was refluxed for 6 h and then kept for evaporation. The light yellow coloured solid metal complex obtained was washed with cold ethanol and water. The synthesis of ligand L2 and metal complex L2M were shown in Scheme 2. Chemical formula: $C_{20}H_{20}C_{l2}MnN_8O_2$, elemental analysis (%): C, 45.30; H, 3.80; N, 21.13; O, 6.03. IR (KBr pellets, υ, cm^{-1}): 1648 (υ C=N), 1354 (υ Ar-H), 1562 (υ N-H); UV-visible absorption [(λ_{max}, nm), solvent, DMSO]: 595, 484, 340 and 235.

Preparation of the microbial culture

The antibiotic tetracyclin was used as a standard in the microbial study and *Bacillus subtilis* as a gram positive bacterium used as the test organism in the yeast surface. The bacteria and the yeast strain were mixed into the nutrient broth (Difco) and malt extract and incubated for more than 48 h. Using disc diffusion method the sterile Mueller Hinton Agar for bacteria and sabouraud dextrose agar for the yeast surface preparation. The synthesised compounds were dissolved in the DMF solvent as 40 (g/disc) solutions and the antibiotic tetracyclin were placed in near the wall (6 mm diameter). The medium was kept under the incubate condition of 32 ºC for 48 h.

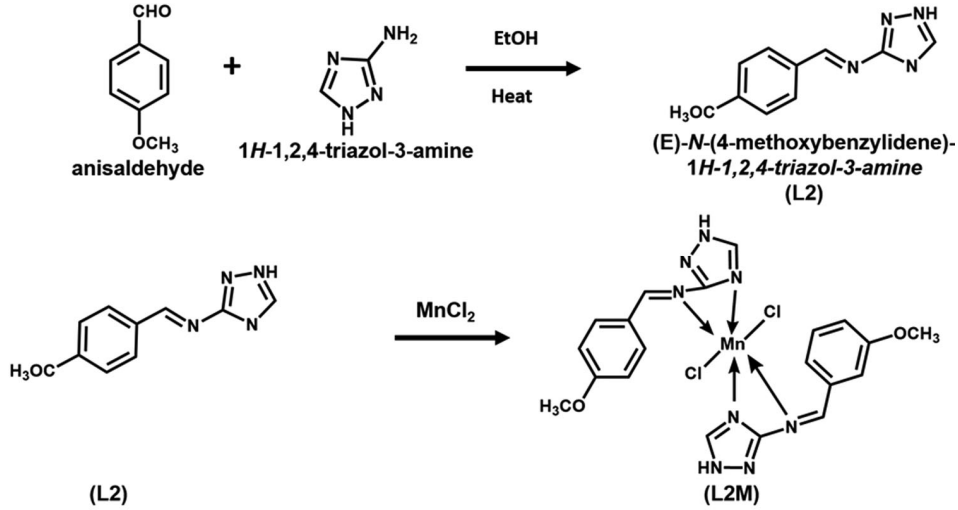
Anticancer cell culture

The monolayer cell culture was trypsinized and the cell count was adjusted to 5.0×10^5 cells/mL using respective media containing 10% FBS. To each well of the 96 well microtiter plate, 100 µL of the diluted cell suspension (50,000 cells/well) was added. After 24 h, when a partial monolayer was formed, the supernatant was flicked off, the monolayer was washed once with medium and 100 µL of different test concentrations of test drugs were added on to the partial monolayer in microtiter plates. The plates were then incubated at 37 ºC for 24 h in 5% CO_2 atmosphere. After incubation the test solutions in the wells were discarded and 100 µL of MTT (5 mg/10 mL of MTT in PBS) was added to each well. The plates were incubated for 4 h at 37 ºC in 5% CO_2 atmosphere. The supernatant was removed and 100 µL of DMSO was added and the plates were gently shaken to solubilize the formed formazan. The absorbance was measured using a microplate reader at a wavelength of 590 nm. The percentage growth inhibition was calculated using the following formula and concentration of test drug needed to inhibit cell growth by 50% (IC_{50}) values is generated from the dose-response curves for each cell line.

Results and Discussion

Characterisation of compounds

The analytical data for the L and metal complexes were listed in the synthesis part. The vibrational spectra explain the functional groups present in the



Scheme 2 — Reaction pathway for L2 and L2M complexes

organic part and also the functionality which involves the coordination for the metal complex formation. In Supplementary Data, Fig. S1(a) shows for L1 the peak at the range of 1650 cm^{-1} represents the C=N functionality and also 1340, 1596 cm^{-1} peaks denotes the aromatic ring and the N-H, respectively. Ligand L2 having FT-IR peak at 1648 cm^{-1} for C=N group denotes the Schiff base formation. A shift in the C=N peak value to 1642 & 1648 cm^{-1} for complex 1 & 2, respectively, confirms the participation of C=N group in metal coordination as shown in Supplementary Data, Fig. S1(b). The ^{1}H and ^{13}C NMR taken in DMSO solvent for ligands L1 and L2 are shown in Fig. 1. For L1, the ^{1}H NMR shows peak at 10.9 ppm range due to the proton present in the C=N (azomethine), the proton of the triazole ring and the benzene ring covers the area of 7.4-8.4 ppm range. The ^{13}C NMR also shows 192 ppm range peak for the azomethine formation and the proton counting covers the total carbon atoms present in the system. In the case of L2, the proton at 7.51 ppm denotes the azomethine formation and at 162 ppm of ^{13}C NMR represents the same functionality.

The electronic spectra for the ligand and complexes were recorded at room temperature using DMSO solvent and are shown in Supplementary Data, Fig. S2. The bands at 375, 328, 272 and 218 for L1 and bands at 370, 322, 265 and 217 nm for L2, can be assigned to π-π^* transition (Supplementary Data, Fig. S2a). In Supplementary Data, Fig. S2b, for the metal complexes the peaks at 573, 595 nm and 460, 484 nm are due to the $^{2}B_2 - {}^{2}B_1$ and also $^{2}B_2 - {}^{2}E_1$ transitions, for L1 and L2, respectively. The ESR spectra of the Mn(II) complexes explains the information about the environmental of the central metal ion which coordinate with the ligand to form the geometry. The ESR spectra of the Mn^{2+} complexes were taken at room temperature and are shown in Fig. 2. The single line of the spectrum for L1M, shows the unpaired electron with two peaks which denotes that the one is for the low field and another is for high field which can be used to calculate $g_{\parallel}$ and $g_{\perp}$ values. For L1M, $g_{\parallel}$ value = 2.432 and $g_{\perp}$=1.397 and for L2M, $g_{\parallel}$ value=2.6390 and $g_{\perp}$=1.950. Based on the results both complexes having $g_{\parallel}$ is greater than $g_{\perp}$. These results indicate that the complexes are in distorted octahedral arrangement.

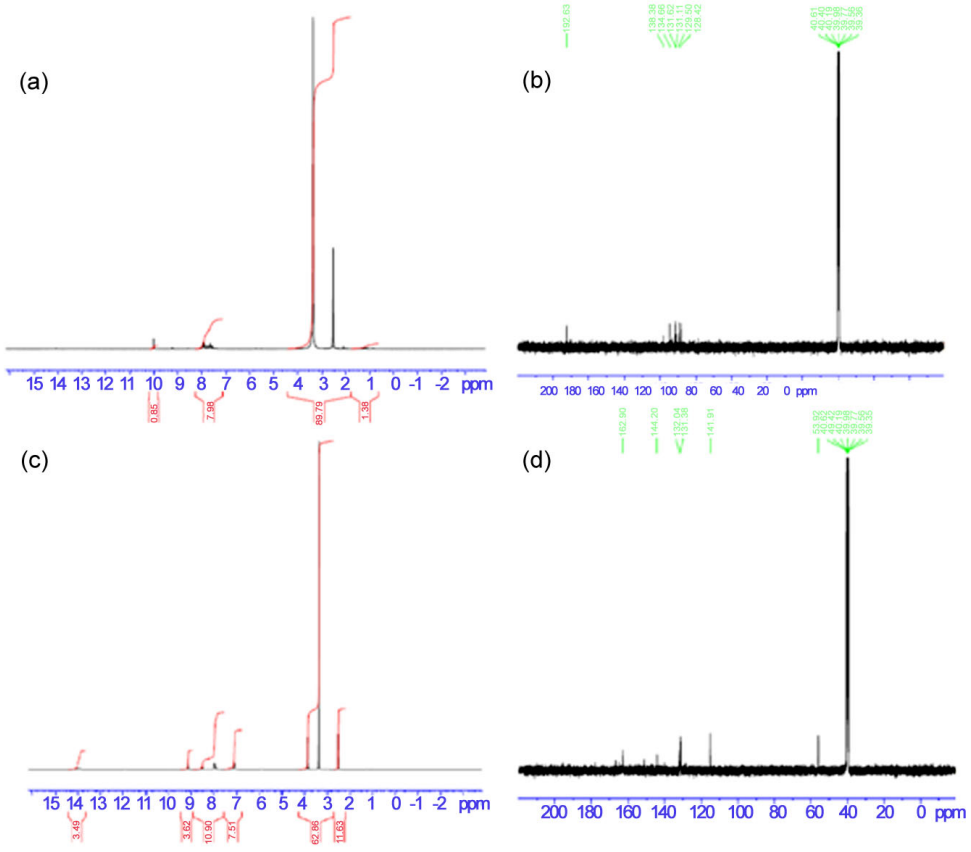


Fig. 1 — ^{1}H NMR spectra for (a) L1, (c) L2, and ^{13}C NMR spectra for (b) L1, (d) L2

Antibacterial activity

Inorganic complex that liberates free radicals can destroy living bacterial cells and cytotoxic potential of these compounds are assessed in terms of zone of inhibition caused by the effective destruction of bacterial colonies. The antibacterial results of the synthesised ligands and compounds were reported in Table 1. The results show that the ligands and the metal complexes were performed against with *Bacillus subtilis* with good activity. The toxicity of the compounds were found to be better activity than the ligand L1 against the *Bacillus subtilis*. The inhibition plot and the antimicrobial activity images were shown in Fig. 3.

Antifungal activity

Newly synthesized Schiff base L1 and L2 and their respective Mn(II) complexes were tested against three fungal strains namely *Phylium Aphanidematum*, *Macrophomina phasiolina*, *Fusarium oxysporum*.

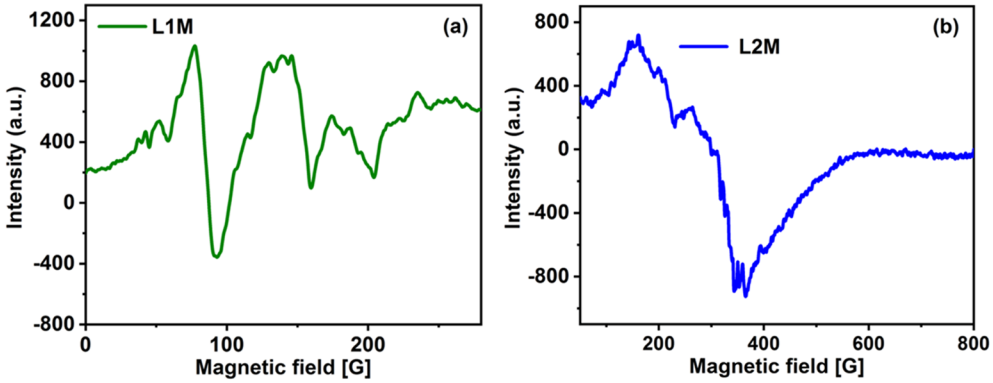


Fig. 2 — ESR spectra for (a) L1M and (b) L2M

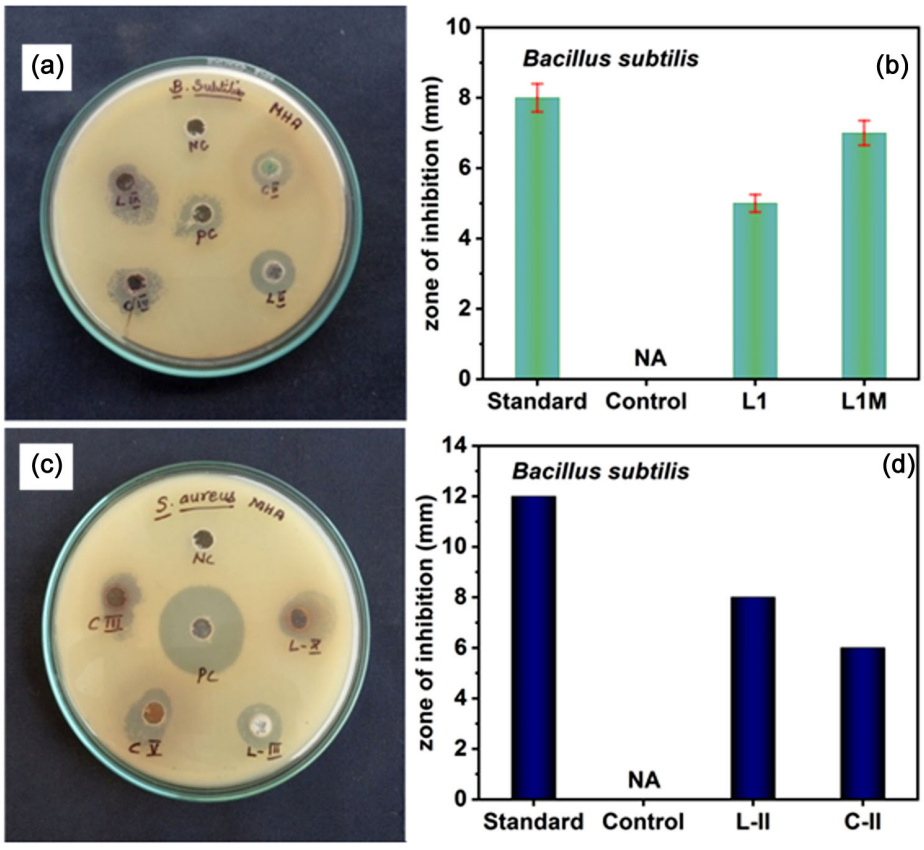


Fig. 3 — Antibacterial activity images and zone inhibition graphs for (a and b) L1 and its complex, and (c and d) for L2 and its complex, respectively

Inhibition rate against each fungi at two different concentrations associated with all four compounds are tabulated in Supplementary Data, Table S1. From results, it is evident that when concentration is increased from 100 to 200 ppm, clearly growth rate of fungi strain is enhanced irrespective of nature of fungus strain. Under the identical experimental conditions, chelation with Mn has improved the inhibition ability, which is attributed due to influence of metal ion upon cellular damage process, which could be better explained with in the light of Tweedy's chelation theory. Lipophilic character of Mn has been enhanced after chelating with ligands due to reduced polarity caused by likely delocalisation of p-electrons that facilitates permeation through the lipid layers of cell membrane of fungi strain. Hence antifungal activity has been improved after co-ordination, consequently both L1M and L2M displayed enhanced rate fungicidal properties in relation to L1 and L2 approximately by 5%.

Table1 — Antibacterial results for L1M and L2M

Sample	Sample concentration (µL)	Zone of inhibition (mm)
	Compound L1M	
Standard	Tetracyclin (10 mg/mL)	8
Control	Ethanol	NA
L1	100	5
L1M	100	7
	Compound L2M	
Standard	Tetracyclin (10 mg/mL)	12
Control	Ethanol	NA
L2	100	8
L2M	100	6

Anticancer activity

The IC50 of a drug can be determined by constructing a dose-response curve and examining the effect of different concentrations of antagonist on reversing agonist activity. IC50 values can be calculated for a given antagonist by determining the concentration needed to inhibit half of the maximum biological response of the agonist. IC50 values for cytotoxicity tests were derived from a nonlinear regression analysis (curve fit) based on sigmoid dose response curve (variable) and computed using Graph Pad Prism. The synthesized compounds were treated with MCF7 tumour cells. The standard reference compound doxorubicin gave the IC50 value of 26.73. The complexes L1M and L2M shows IC50 value 81.86 and 200.6, respectively, as shown in Supplementary Data, Table S2. The result shows complex L1M shows better activity towards MCF7 cell than L2M (Fig. 4 and Table 2). Anticancer cell

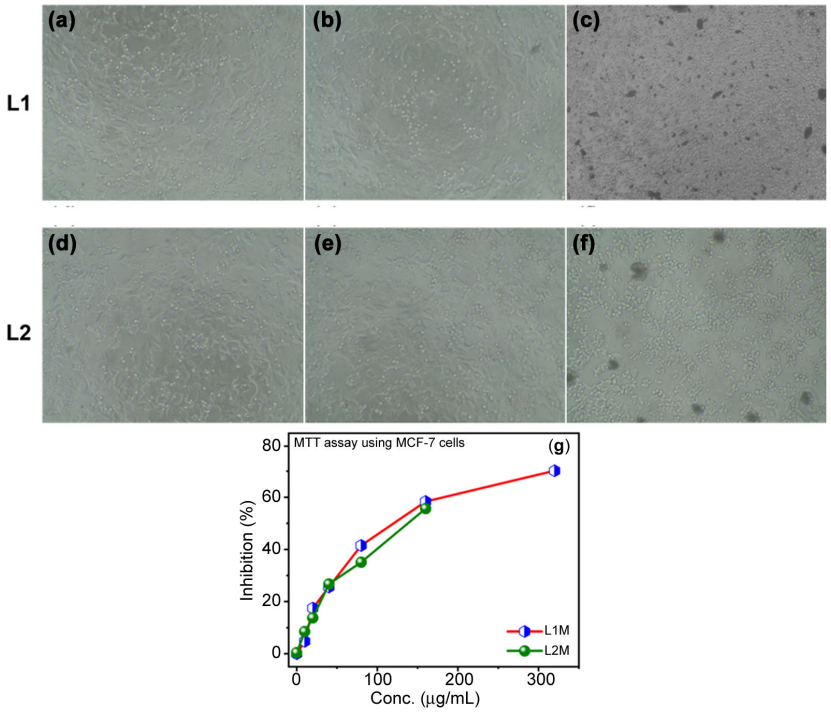


Fig. 4 — Images showing anticancer activities (a, b, c) for L1M and (d, e, f) for L2M using Control, 10 ug/mL, 320 µg/mL of compounds, respectively, and (g) plot of concentration versus % inhibition complexes

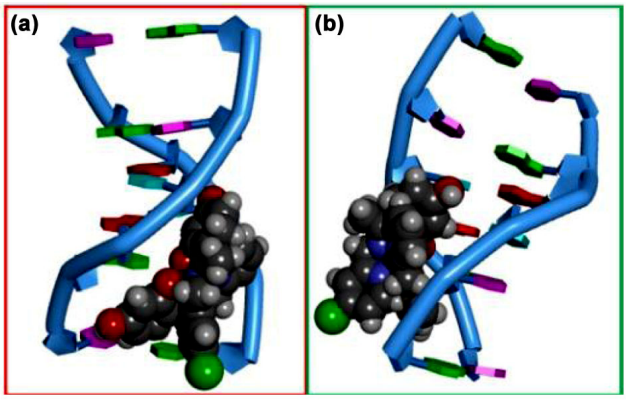


Fig. 5 — Molecular docking results of (a) L1M and (b) L2M

Table 2 — Anticancer results against MCF-7 cell lines

Compound	Conc. (g/mL)	OD@590 nm	% Inhibition	IC50 (g/mL)
Control	0	0.778	0.00	81.86
L1M	10	0.741	4.76	
	20	0.642	17.48	
	40	0.579	25.58	
	80	0.455	41.52	
	160	0.324	58.35	
	320	0.232	70.18	
L2M	10	0.775	0.39	200.6
	20	0.712	8.48	
	40	0.671	13.75	
	80	0.57	26.74	
	160	0.505	35.09	
	320	0.345	55.66	

line testing with MCF 7 studies are shown in Supplementary Data, Fig. S3, indicated that these complexes arrested the cell cycle efficiently and promoted tumour cell destruction *via* a reactive oxygen species (ROS)-mediated mitochondrial pathway. Further the complexes were evaluated for DPPH radical scavenging activity. The IC50 values were found to be 0.180, 0.196 mg/mL for L1M, L2M, respectively (Supplementary Data, Table S3).

Molecular Docking Studies with DNA

Many recent reports have described the biological applications of Manganese-coordinated complexes and pronounced consideration has been paid to their excellent potency as anti-tumour drugs. Mode of drug binding and its interaction with specific biomolecule (DNA/Protein) could be evaluated through molecular modelling of drugs. Herein we attempted to provide better insight about interaction of synthesised complex with DNA that serve as a widely used therapeutic target for diseases concerning intracellular interactions. In DNA, hydrogen bonding interaction is predominantly noticeable for adenine–thymine and guanine–cytosine base pairs in the complementary double helix structure. Graphical representation of the interaction model of complex with DNA is as shown in Supplementary Data, Fig. S4.

Molecular docking studies were performed for docking and interaction calculations for categorising the probable binding sites for the drug molecules. The synthesized Mn(II) complexes used to dock with DNA hexamer d(CGATCG)2 (PDB ID: 1Z3F). Using this molecular docking study, we can predict the complex–biomolecular interaction and it plays vital role in the drug discovery and also it is a step by step process which used to place synthesised compounds into the binding sites of the DNA molecule. The complexes exhibit intercalation mode of binding towards the DNA molecule by considering the binding mode and binding affinity. The binding interactions of drug-DNA are -5.9 and -5.5, respectively, for complex L1M and L2M. Overall results suggests that the synthesized complexes have the tendency to bind with the DNA molecule, as L1M is having the lowest binding energy value so it strongly binds with the DNA molecule (Fig. 5).

Conclusions

Organometallics based drugs are proposed for many therapeutic applications and this study attempted a manganese complex as a new drug and demonstrated its use for treating MCF7 carcinogenic cells. Two novel Schiff base ligands (L1 and L2) and based on synthesised ligands Mn(II) co-ordination complexes (L1M and L2M) were synthesised. The structures of these compounds were elucidated by FT-IR, UV-Vis, NMR and ESR characterisation techniques. Developed Mn(II) complexes showed good oxidative stability along with high antibacterial activity when tested against the gram positive bacterium *Bacillus subtilis*. Antifungal activity has been improved after co-ordination, consequently both L1M and L2M displayed enhanced rate fungicidal properties in comparison to L1 and L2 approximately by 5%. In addition, the results show that it is possible to tailor the desired Schiff base through condensation with triazole derivative. Using the molecular docking study, we can predict the complex–biomolecular interaction and it plays vital role in the drug discovery and also it is a step by step process which used to place synthesised compounds into the binding sites of the DNA molecule. The

synthesised compounds were treated with MCF7 cancer cell and the L1M shows better activity towards the cell line. These studies indicated that these complexes arrested the cell cycle efficiently and promoted tumour cell destruction *via* a reactive oxygen species mediated mitochondrial pathway. Further, Molecular DNA docking results demonstrated encouraging responses, thereby opening up new avenues for the application of the synthesized inorganic triazole derivative complexes as leads for the development of novel anti-cancer drugs.

Supplimentary Data

Supplementary data associated with this article are available in the electronic form at http://nopr.niscair.res.in/jinfo/ijca/IJCA_60A(06)797-805_SupplData.pdf.

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References

1 World Trade Organization, World Health Organization, and World Intellectual Property Organization, *Promoting Access to Medical Technologies and Innovation: Intersections Between Public Health, Intellectual Property and Trade* WTO (2013).
2 M07: Dilution AST for Aerobically Grown Bacteria - CLSI.
3 Santos AF, Brotto DF & Favarin LRV, *Revista Brasileira de Farmacognosia*, 24 (2014) 309.
4 Souza P, Garcia-Vzquez J A & Masaguer J R, *Transition Met Chem*, 10 (1985) 410.
5 Shavit M, Pokrovskaya V, Belakhov V & Baasov T, *Bioorg Med Chem*, 25 (2017) 2917.
6 Santos A F, Brotto D F & Favarin L R V, *Revista Brasileira de Farmacognosia*, 24 (2014) 309.
7 Index of subjects, *J Chem Soc A*, (1967) 2131.
8 Coto V, Souza P, Masaguer J R & Arquero A, *Transition Met Chem*, 11 (1986) 373.
9 García C P, *Rev Chil Infectol*, 20 (2003).
10 Tümer M, Koksal H, Sener M K & Serin S, *Transition Met Chem*, 24 (1999) 414.
11 Gokel G W & Murillo O, *Acc Chem Res*, 29 (1996) 425.
12 Rohrschneider L, *Anal Chem*, 45 (1973) 1241.
13 Mostafa M M, El-Hammid A, Shallaby M & El-Asmy A A, *Transition Met Chem*, 6 (1981) 303.
14 Raymond K N & Basolo F, *Inorg Chem*, 5 (1966) 1632.
15 Jansen A H, Russell B J & Chernick V, *Canadian J Physiol Pharmacol*, 53 (1975) 726.
16 Fyhn H J, *Comp Biochem Physiol A Comp Physiol*, 53 (1976) 19.
17 Tumer M, Koksal H, Sener M K & Serin S, *Transition Met Chem*, 24 (1999) 414.
18 Reichling J, Koch C, Stahl-Biskup E, Sojka C & Schnitzler P, *Planta Med*, 71 (2005) 1123.
19 Bhagwat V M & Ramachandran B V, *Biochem Pharmaco*, 24 (1975) 1713.
20 Lakings D R, Gehrke C W & Waalkes T P, *J Chromatogr*, 116 (1976) 69.
21 Geigy R, Jenni L, Kauffmann M, Onyango R J & Weiss N, *Acta Trop*, 32 (1975) 190.
22 Supuran C T, Barboiu M, Luca C, Pop E, Brewster M E & Dinculescu A, *Eur J Med Chem*, 31 (1996) 597.
23 Sumrraa S H, Ramzana S, Mustafaa G, Ibrahim M, Mughala E. U., Nadeem M A, Chohand Z H & Khalide M, *Russian J Chem*, 88 (2018)1707.
24 Shen S, Chen H, Zhu T F, Ma X Q, Xu J, Zhu W J, Chen R H, Xie J, Ma T L, Jia L, Wang Y & Peng C Y, *Oncol Lett*, 13 (2017) 3169.
25 Keypour H, Ansari N, Mahmoudabadi M, Karamian R, Farida S H M, Moghadam M E & Gable R W*, Inorg Chim Acta,* 509 (2020) 119705.
26 Ispir E, Toroglu S & Kayraldiz A, *Transition Met Chem*, 33 (2008) 953.
27 Maryam Damercheli, Davood Dayyani, Mahdi Behzad, Bita Mehravi & Mehdi Shafiee Ardestani, *J Coord Chem,* 68 (2015) 1500.