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SYNTHESIS CHARACTERIZATION AND MOLECULAR DOCKING STUDY OF SELECTED COMPOUNDS ON ANTIBACTERIAL AND ANTIFUNGAL ACTIVITIES

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ABSTRACT

Objective: The development, characterization and molecular docking of novel antibacterial agents. Schiff bases are reported to possess a broad range of pharmacological activities, which also include antibacterial, antifungal activity etc. With this background, novel Schiff bases were synthesized. **Method:** To synthesize characterization the of Schiff base legend and Metal complex, molecular docking study help to improve the already available drugs potential and also helps to synthesise novel drugs for the suitable biomolecular target area. The synthesised metal complexes were used to dock with the DNA hexamer unit and amino acid units. **Result and Conclusion:** The present study provides information in respect of The metal complexes were synthesized using the backbone of Schiff base ligands and characterized using spectral techniques like UV-Vis, FT-IR. One of the ligand was isolated in crystal forms which give the exact structure of the particular compound and additionally supports the formation of metal complexes using the moiety. The spectrum of the copper complexes explains the paramagnetic nature. The structures are confirmed by various spectral methods. The molecular docking study supports the binding nature of the synthesized complexes with biomolecule. The antifungal and antibacterial result of the metal complexes explains such compounds acts like potential anti infection drugs.

KEYWORDS: molecular docking, biomolecular, antibacterial, Schiff base, ligand.

1. INTRODUCTION

Compounds having an azomethine group are Schiff bases or Schiff's base which are formed by the condensation of aldehydes and/or ketones with primary amine, this reaction was first discovered in 1864[1] by Hugo Schiff a German chemist[2] and Nobel Prize winner, and contain carbon nitrogen double bond. In these compounds the nitrogen atom in carbon nitrogen bond is not bonded to hydrogen atom, but bonded to alkyl or aryl group. Usually Schiff bases are formed under acid or base catalysis or in hot condition. In Schiff base which is an analogue of aldehydeor ketone where the carbonyl group in aldehyde or ketone is replaced by an imine group.[3,4,5] The general mechanism of the Schiff base is given in reaction scheme fig.1. The fundamental schiff base is crystalline solids, are weakly essential. Usually schiff base utilized as intermediates for the combination of amino acids or as ligands for the preparation of metal buildings having a progression of various structures.

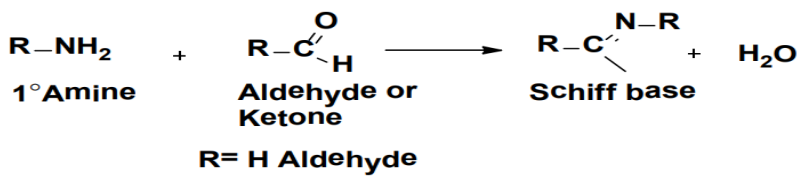


Fig. 1: Reaction scheme.

Besides six metal ions can hold 4 ligands which has a large central hole in which guestmolecules can be placed is synthesized.[6]

Sweet-smelling aromatic aldehydes particularly with a successful conjugation framework form stable Schiff bases, whereas those aliphatic aldehydes are unstable and readily polymerize.[7,8,9] Schiff base ligands with ketones are less readily formed than with aldehydes. Schiff bases have incredibly flexible and diverse structures.

Schiff base ligands have significant importance in biochemistry; especially in the development of schiff base complexes, because Schiff base complexes are capable of forming new stable complexes with the transition ions and many Schiff base metal complexes show excellent catalytic activity in various reactions at a higher temperature and in the presence of a catalyst.[10,11] Over the past recent years, there have been much works of literature based on their applications in homogeneous and heterogeneous catalysis, hence the need for a review article highlighting the catalytic activity of Schiff base metal complexes.[12]

2. MATERIALS AND METHOD

All the chemicals used in the present work were purchased from commercial sources (AR Grade). Pyridoxal hydrochloride (Assay 99%), o-vanillin (Assay 99%), ethanolamine (Assay 98%), 4-aminoantipyrine (Assay 97%), 3,5- dichlorosalicylaldehyde (Assay99%), copper perchlorate (Assay 98%), nickel perchlorate (Assay 97%), zinc perchlorate (Assay 97%), copper chloride (Assay 99.99%), nickel chloride (Assay 99.99%), zinc chloride (Assay 99.99%) and vanadyl sulphate salts (Assay 97%) were bought from Sigma Aldrich, USA and used as received.

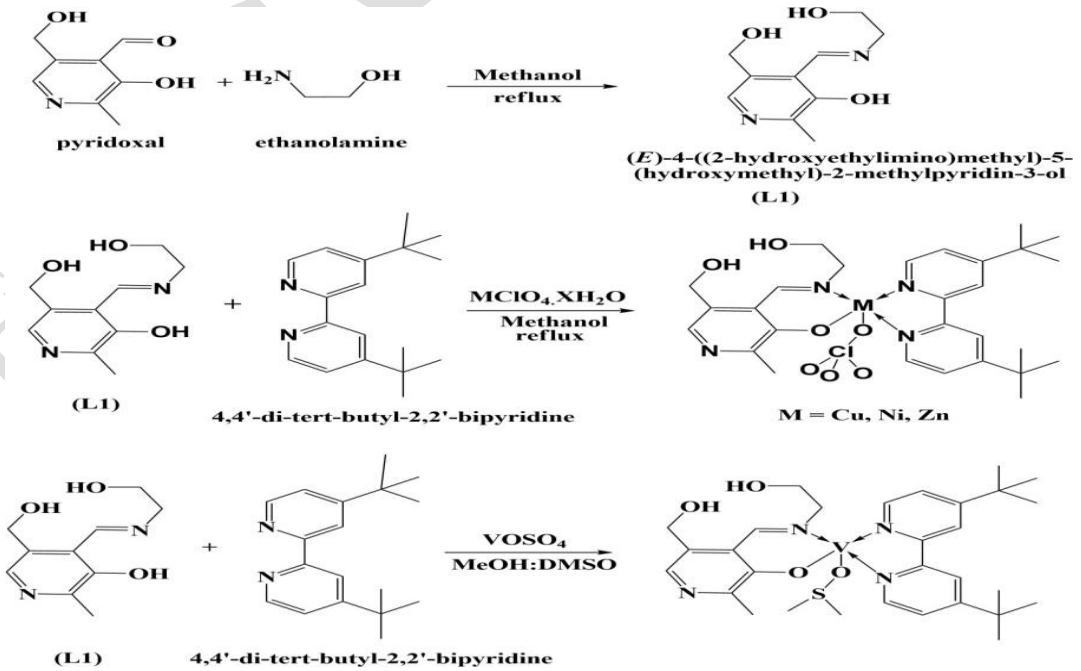
Solvents like CDCl3, acetonitrile, methanol, chloroform, ethanol, and DMSO used in the present research were bought from Merck and commercial source (AR Grade).

2.1 Synthesis of Schiff base (L1), (E)-4-((2-hydroxyethylimino)methyl)-5- (hydroxyl methyl)-2-methyl pyridine-3-ol

Schiff base (L1) was synthesized by the condensation reaction between pyridoxal hydrochloride (1mmol) and ethanolamine (1mmol). Both the reactants were dissolved in methanol solvent and refluxed for 3 hours. A yellow solution of Schiff base was formed. The reaction mixture was further used for the metal complex synthesis.[13,14]

2.2 Synthesis of the complexes of L1, [M L1] M = Cu(II), Zn(II), Ni(II) and VO(II) Complexes (1-4), General procedure

Metal complexes were synthesized by template method. The methanolic solution of L1 (1mmol) was treated with metal salts [(Cu, Ni and Zn) perchlorates and Vanadyl sulphate)] (1mmol) which was dissolved in 5ml of methanol. 4,4'-ditert-butyl-2,2'-bipyridine (1mmol) was added drop wise into the reaction mixture and refluxed the solution for 5 hours. Colored insoluble solid mass were appearing within one hour.[15] The solid mass was filtered and washed with 5 ml cold methanol. For copper complex a green color, nickel complex a red color, zinc complex pale yellow and vanadium yellow color solid obtained. The solutions are kept into the deep freeze for 5 days. A crystalline particle appeared. Crystals were washed with cold methanol and diethyl ether solution and carried out for further analysis.[16-17]



Scheme 1: Systematic representation of complexes.

2.3 Synthesis of Copper (II) L1 metal complexes

Copper perchlorate (1mmol), 4,4'-di-tert-butyl-2,2'-bipyridine (1mmol) and L1 (1mmol), stirred for 1 hour, colour of the complex – green, yield (83%). Chemical formula: C28H37N4O7ClCu. Elemental analysis: C, 52.50; H, 5.82; Cl, 5.53; Cu, 9.92; N, 8.75; O, 17.48 %. IR (KBr pellets) υ cm-1 :2958 (υ C-H), 1625 (υ C=N), 508 (υ Cu-N). Mass spectra: 644.35 m/z base peak (M+3).[18]

2.4 Synthesis of Nickel (II) L1 metal complexes

Nickel perchlorate (1mmol), 4,4'-di-tert-butyl-2,2'-bipyridine (1mmol) and L1 (1 mmol), refluxing time 1 hour, colour of the complex –red, yield (79%) Chemical formula: C28H37N4O7ClNi. Elemental analysis: C, 52.90; H, 5.87; Cl, 5.58; N, 8.81; Ni, 9.23; O, 17.62 %. IR (KBr pellets) υ cm-1 :2955 (υ C-H), 1617 (υ C=N), 521 (υ Ni-N). Mass spectra: 639.37m/z base peak (M+3).[19]

2.5 Synthesis of Zinc (II) L1 metal complexes

Zinc perchlorate (1mmol), 4,4'-di-tert-butyl-2,2'-bipyridine (1mmol) and L1 (1 mmol), refluxing time 1 hour, colour of the complex –pale yellow, yield (74%). Chemical formula: C28H37N4O7 ClZn. Elemental analysis: C, 52.34; H, 5.80; Cl, 5.52; N, 8.72; O, 17.43; Zn, 10.18%. IR (KBr pellets) υ cm-1 :2980 (υ C-H), 1619 (υ C=N), 539 (υ Zn-N). Mass spectra: 645.38m/z base peak (M+3).

2.6 Synthesis of Vanadium (IV) L1 metal complexes

Vanadyl sulphate (1mmol), 4,4'-di-tert-butyl-2,2'-bipyridine (1mmol) and L1 (2.32g, 10mmol), refluxing time 1 hour, colour of the complex –yellow, yield (85%). Chemical formula: C30H43N4O4SV. Elemental analysis: C,59.39; H,7.14; N,9.23; O, 10.55; S, 5.29; V, 8.40%. IR (KBr pellets) υ cm-1 :2982 (υ C-H), 1622 (υ C=N), 560 (υ V-N). Mass spectra: 619.39m/z base peak (M+3).

3. Characterization of Synthesize Drug

3.1 Elemental analysis of the complexes

Samples of complexes are analysed for the elements present and the experimental values are found to agree with the calculated values.[21] Colour and elemental composition of the complexes are given in table.

Table 1: Physical and analytical data of complexes.

Molecular formula of the Complex	Molecular weight (a.m.u)	Colour	Elemental composition			
			Found (calculated)			
			%C	%H	%N	%Metal
$C_{28}H_{37}N_4O_7ClCu$[1]	642.11	Green	52.50	5.82	8.75	9.92
			(52.61)	(5.81)	(8.72)	(9.90)
$C_{28}H_{37}N_4O_7ClNi$ [2]	637.26	Red	52.90	5.87	8.81	9.23
			(53.00)	(5.85)	(8.79)	(9.21)
$C_{28}H_{37}N_4O_7ClZn$[3]	643.95	Pale yellow	52.34	5.80	8.72	10.18
			(52.45)	(5.79)	(8.70)	(10.15)
$C_{30}H_{43}N_4O_4SV$[4]	608.29	Yellow	59.39	7.14	9.23	8.40
			(59.50)	(7.12)	(9.21)	(8.37)

3.2 FT-IR Spectroscopy

The Fourier Transform Infrared Spectrophotometer (FT-IR) spectra for the synthesized ligands and metal complexes were recorded using Shimadzu FTIR-8400S model. The samples were converted in the form of pellets using KBr and the spectra covers in the range of 4000-400 cm-1.[22]

FT-IR is one of the best tools to determine the nature of the functional group present and the formation of new complex from the reactant molecule. Complex C28H37N4O7ClCu, shows the absorption bands at 2958 cm-1 corresponding to C-H stretching in aryl group, at 1625 cm-1 corresponding to >C═N showing the presence of azomethine bond and the formation of metal ligand bond at the frequency 508 cm-1. Ring stretching vibration is observed in the range 1600-1500 cm-1. C-H stretching in methyl group is seen at the frequency 2825 cm-1, a peak near 1100 cm-1 with splitting is due to coordinated perchlorate ion. The peak at 3448-3138 cm-1 is due to OH group of the pyridoxal ligand. A band at 1390 cm-1 shows the presence of t-butyl group.[23,24]

Table 2: IR spectral data of complexes.

Sample	υC-H(cm^{-1})	υC=N(cm^{-1})	υM-N(cm^{-1})
$C_{28}H_{37}N_4O_7ClCu$[1]	2958	1625	508
$C_{28}H_{37}N_4O_7ClNi$ [2]	2955	1617	521
$C_{28}H_{37}N_4O_7ClZn$[3]	2980	1619	539
$C_{30}H_{43}N_4O_4SV$[4]	2982	1622	560

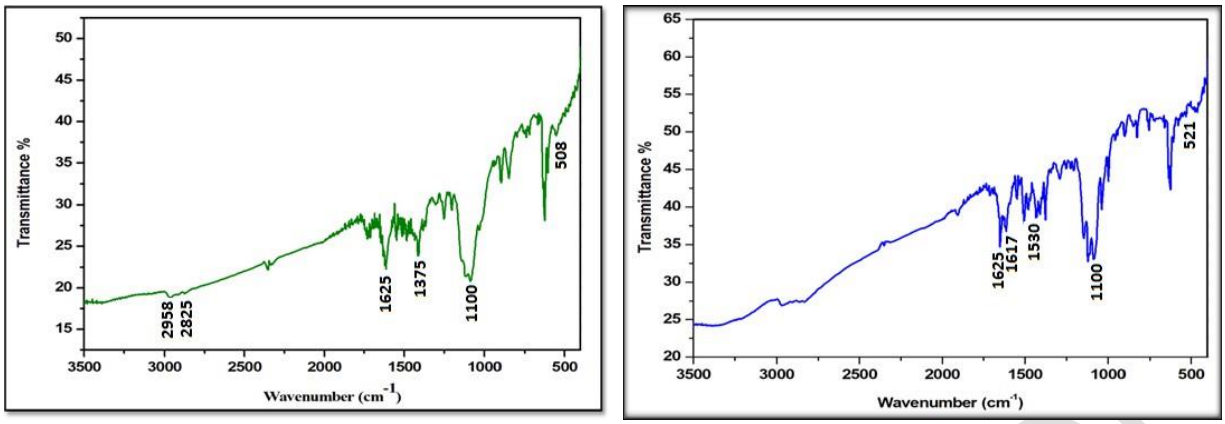


Fig. 2: IR spectrum of complex, C28H37N4O7ClCu [1] and C28H37N4O7Cl Ni [2]

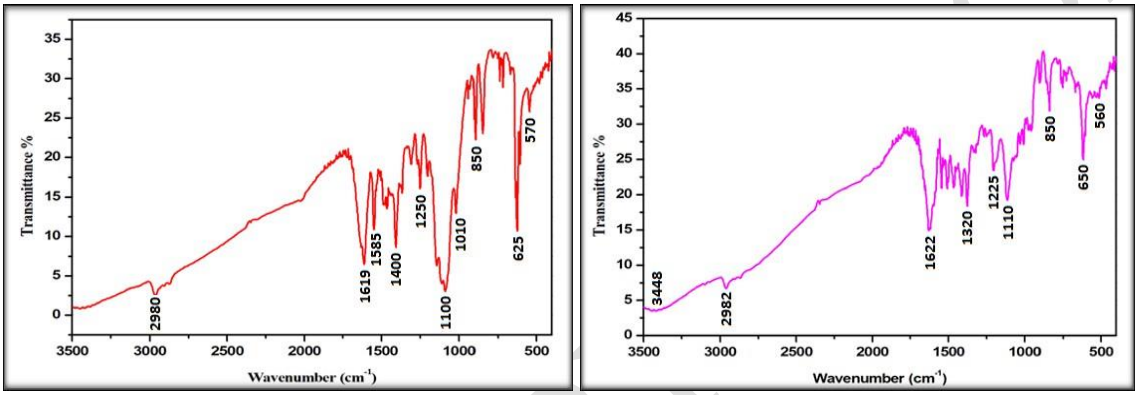


Fig.3: IR spectra of complex C28H37N4O7ClZn [3] and C30H43N4O4SV [4]

3.3 UV spectral analysis of complexes

The electronic absorption spectra was taken using DMSO solvent. The spectrums were taken in the range of 200-700 nm. The electronic spectrum of copper complex C28H37N4O7ClCu shows the absorption peaks at 223, 289, 342 and 648 nm which represent respectively π- π*, n- π*, LMCT and also 2Eg →2T2g transition. The L→M charge transfer transition and d-d transition of metal ion (2Eg→2T2g) clearly shows the distorted octahedral structure which indicates the square pyramidal geometry.[25-26]

The spectra for Nickel complex C28H37N4O7Cl Ni having the peak at 231, 280, 335, 403 and 640 nm which clearly shows the respective electronic transition given in the table 5.4. From the electronic transition, we can understand the d-d transition 3A1g→1B2g and 1A1g→1B1g at 403 nm and 640 nm shows square pyramidal geometry of the nickel (II) complex. 200-203.The electronic spectra of Ni(II) complex (2) has the peaks at 231 nm which corresponds to π→π* transition, 280nm corresponds to n→π* transition,335 nm is due to ligand to metal charge transfer.[27]

The zinc complex C28H37N4O7ClZn shows the electronic spectra in the range of 248, 325 and 419 nm having the electronic transition of π- π* and n- π* respectively. Complex 3 is a five coordinated zinc (II) metal complex and having square pyramidal geometry.[28]

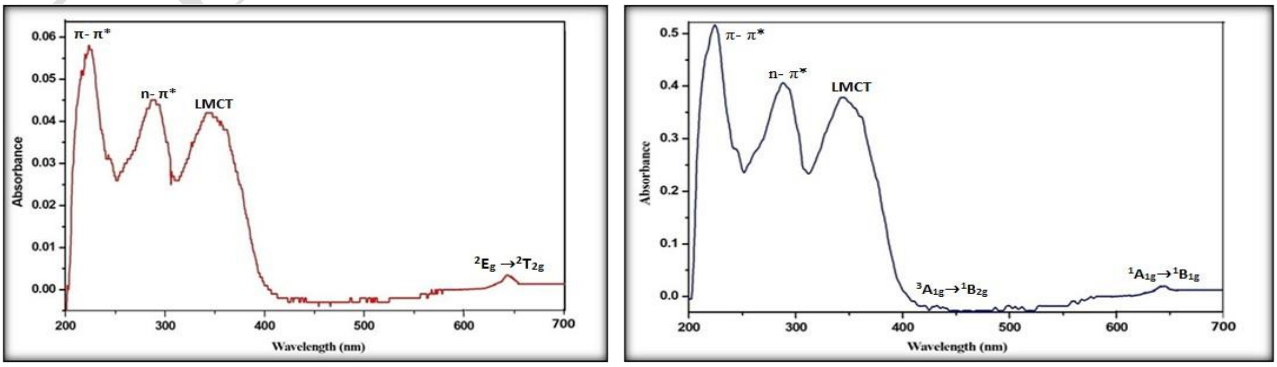


Fig- UV-Vis spectrum of complex, C28H37N4O7ClCu and C28H37N4O7ClNi.

Vanadium Complex, C30H43N4O4SV having +4 oxidation state of the vanadium metal ion and also the spectra at 217nm, 287nm, 359nm, 450nm and 572nm. The absorption bands represents the n- π*, LMCT, 3A1g→1B2g and 1A1g→1B1g. The ligand metal (d-d) charge transfer represents the square pyramidal geometry structure. Absorption band at 572nm is due to electronic transition from dxy to dx2-y2. 210. To conclude, all the metal complexes (1-4) are having square pyramidal structure.[29]

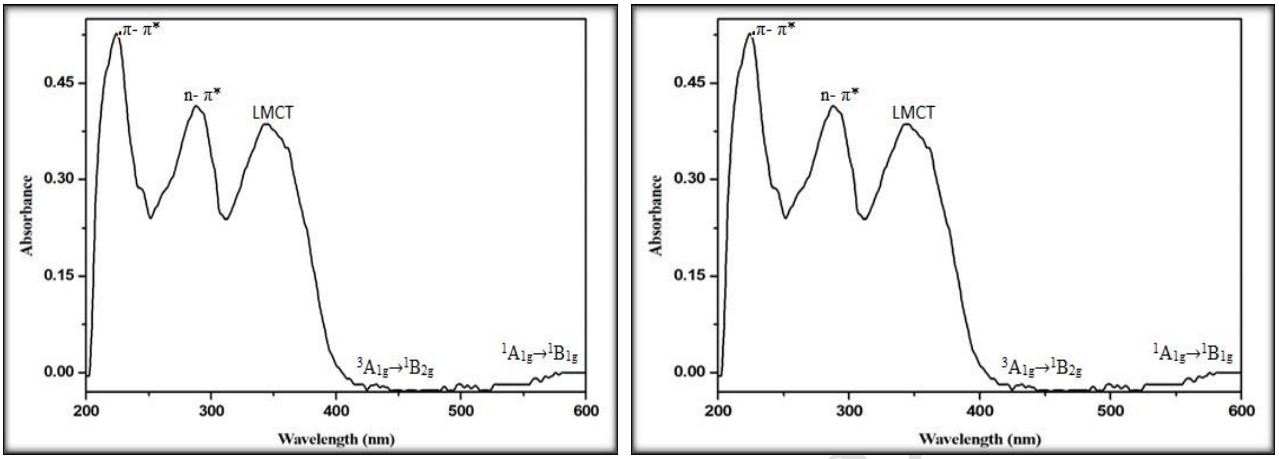


Fig- UV-Vis spectrum of complex C28H37N4O7ClZn and C30H43N4O4SV.

The electronic absorption spectrum (UV-Vis) data of metal complexes 1-4 were reported in the table and the corresponding spectrum images were shown in the Fig.

Table 3: UV spectral data for complexes (1-4).

Compound	λ_{max}(nm)	Assignment
$C_{28}H_{37}N_4O_7ClCu$ [1]	223 289 342 648	π- π* n- π* LMCT $^2E_g\rightarrow{}^2T_{2g}$
$C_{28}H_{37}N_4O_7ClNi$ [2]	231 280 335 403 640	π- π* n- π* LMCT $^3A1g\rightarrow{}^1B2g$ $^1A1g\rightarrow{}^1B1g$
$C_{28}H_{37}N_4O7ClZn$[3]	248 325 419	π-π* n-π* n- π*
$C_{30}H_{43}N_4O_4SV$ [4]	217 287 359 450 572	π- π* n- π* LMCT $^3A1g\rightarrow{}^1B2g$ $^1A1g\rightarrow{}^1B1g$

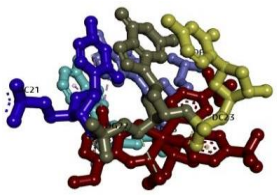
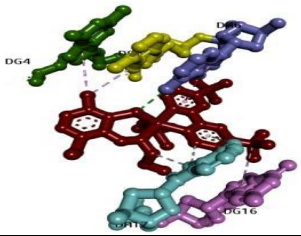
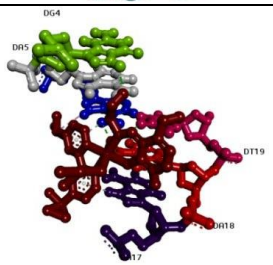
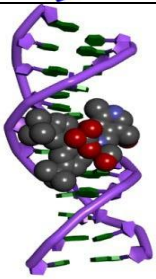
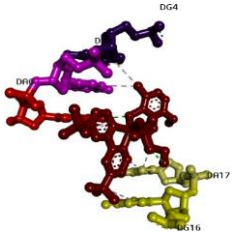
4. Molecular docking studies

Molecular docking study is one of the best tools to understand the drug biomolecular interaction. This study help to improve the already available drugs potential and also helps to synthesise novel drugs for the suitable biomolecular target area. The synthesised metal complexes were used to dock with the DNA hexamer unit d(CGATCG)2 bi-functional enzyme B-DNA (PDB ID: 1BNA). All the synthesized complexes exhibits intercalation mode of binding towards the targeted DNA molecule by considering the binding mode and the binding affinity. There will be nine possible conformers which the molecule attacks at nine different positions towards the DNA.[30]

Table 4: Molecular docking studies with BDNA molecule.

Complex	Acceptor group	Donor group	Binding energy (kcal mol^{-1})	Distance (Å)
$C_{28}H_{37}N_4O_7ClCu$[1]	O7	DA6	-6.6	3.18
	C13	DA17		3.40
	C16	DA17		3.68
	C10	DG4		4.37
$C_{28}H_{37}N_4O_7ClNi$[2]	O40	DA6	-6.5	3.13
	O40	DA6		3.35
	C5	DG22		3.64
$C_{28}H_{37}N_4O_7ClZn$[3]	O15	DA5	-8.1	2.28
	O15	DA6		2.17
	O7	DT19		2.37
	O37	DA6		2.77
$C_{30}H_{43}N_4O_4SV$[4]	C10	DG4	-6.2	4.21
	C10	DA5		4.92
	C13	DA17		3.38
	C28	DG16		5.19

In complex 1, the acceptor group binds with the donor group at a distance of 3.18 Å with the binding energy -6.6.Kcal/mole. Complex 2 binds at a distance of 3.13 Å, the acceptor group being O40 and the donor group is DA6. the binding energy for this complex is -6.5Kcal/mole. In the zinc complex, the binding energy is 8.81Kcal/mole, where the acceptor and donor group are O15 and DA5 respectively.C10 which is the acceptor group in vanadium complex binds with the donor group DG4 with the binding energy of -6.2Kcal/mole.[32]

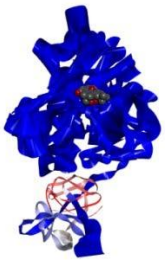
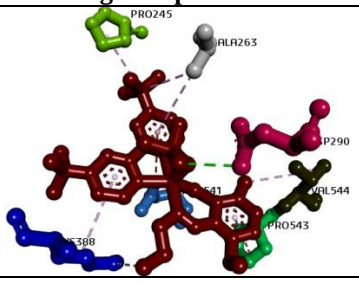
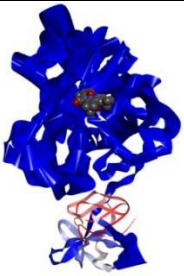
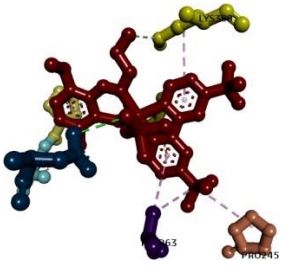
Complex	BDNA	Docking Complex Structure
$C_{28}H_{37}N_4O_7ClCu$ [1]		
$C_{28}H_{37}N_4O_7ClNi$ [2]		
$C_{28}H_{37}N_4O_7ClZn$[3]		
$C_{30}H_{43}N_4O_4SV$[4]		

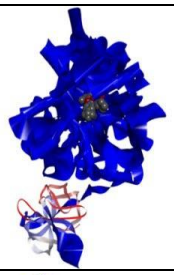
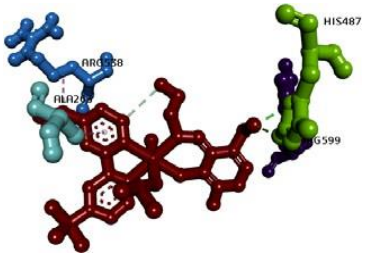
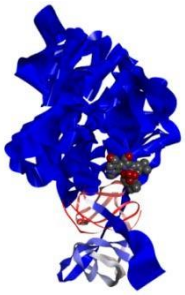
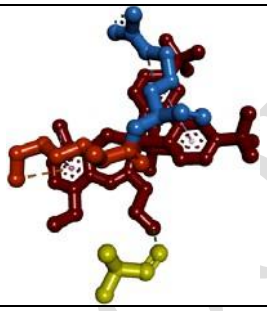
The complexes interact with DA6, DA17, DG4, DG22, DG23, DA5, DT19, DG4, DG16, DT7, DC21, DC24 and DT8 nucleotide of the DNA molecule. From the docking results complex 3 having great interaction and having great binding energy value.

Table 5: Molecular docking results of complexes (1- 4) with BSA protein biomolecule.

Complex	Acceptor group	Donor group	Binding energy (kcal mol^{-1})	Distance (Å)
$C_{28}H_{37}N_4O_7ClCu$[1]	O39	ASP290	-7.4	3.27
	O15	LYS388		3.59
	C29	ALA263		4.13
	C10	VAL544		4.72
	C29	PRO245		4.82
$C_{28}H_{37}N_4O_7ClNi$[2]	O39	ASP290	-7.2	3.25
	N2	PRO543		3.49
	O15	LYS388		3.62
	C29	ALA263		4.18
	C29	PRO245		4.78
$C_{28}H_{37}N_4O_7ClZn$[3]	O12	HIS487	-8.1	2.64
	O12	ARG599		2.36
	C28	ARG538		4.58
	C21	ALA263		4.32
$C_{30}H_{43}N_4O_4SV$[4]	O15	ALA234	-7.1	3.28
	C10	LYS210		4.57
	C25	ARG202		4.44
	C21	ARG202		3.56

The synthesized metal complexes (1-4) interact with the dengue protein Dengue NS3 protease-helicase (PDB ID: 2VBC) biomolecule. There are two side chains present in the target receptor. Using docking study we can analyse the binding energy, binding mode and the binding interaction of the drug – protein. There are nine possible conformers available. The best mode of binding is selected and shown in the fig.5.21. Several amino acid residues were involved in the binding study and they are ASP290, LYS388, ALA263, VAL544, PRO245, ASP290, PRO543, LYS388, ALA263, PRO245, HIS487, ARG599, ARG538, ALA263, ALA234, LYS210, ARG202, ARG202, ALA606, ASP290, HIS487, ASP409, PRO543, ALA602, ALA606, PRO543, ARG599, ASP409, ARG387, ASP409, LEU429, HIS487, ARG599, PRO543, ASP290, ARG599, ALA606, HIS487, ASP409, THR289, ALA452, SER453, LYS430, ARG599, LEU443, PRO291, HIS487, ASP409, HIS487, PRO431, PRO543, ALA406,CYS292, PRO291, ALA606, LEU429, HIS487, ALA602, ALA606, PRO543, ASP409 and HIS487. The amino acid residues interacted by the drug atom by using pi-alkyl, pi-pi stacked, H-bonding and Vander Waals weak interactions. The interaction values and the mode were noted in the table.[33,34]

Complex	NS3 protease-helicase	Docking Complex Structure
$C_{28}H_{37}N_4O_7ClCu$ [1]		
$C_{28}H_{37}N_4O_7ClCu$ [2]		

$C_{28}H_{37}N_4O_7ClZn$ [3]		
$C_{30}H_{43}N_4O_4SV$[4]		

5. Antimicrobial and larvicidal activity studies of complexes

Recently, considerable attention is given to exploit the antibacterial properties shown by the chemically synthesized metal ions against several human pathogenic bacteria, which are known to cause infection to humans as well as to aquatic organisms. Bacteria are commonly found in human skin and gastrointestinal tract. It also causes skin and soft tissues infections, invasive diseases, sepsis etc. However, the indiscriminate use of antibiotics against their bacteria to safe guard the human health and other organisms is resulting not only in the development of disease resistant bacteria but also in their accumulation in human tissues, plant products (vegetables, fruits etc.) ultimately finding their way to human beings who consume it.[35,36]

Therefore, alternatives for chemical antibiotics are needed. In recent years, a rapid increase in microbes that are resistant to conventionally-used antibiotics has been observed. Antifungal drug therapy is no exception; resistant to many of the antifungal agents now in use has emerged. Although antifungal drug resistance does not seem to be as much of a problem as resistance to antibacterial agents in bacteria, one long-term concern is that the number of fundamentally different types of antifungal agents that is available for treatment remains extremely limited. This is because fungi are eukaryotic organisms with a structure and metabolism that are similar to those of eukaryotic hosts. Therefore, there is an inevitable and urgent medical need for antibiotics with novel antimicrobial agents.[37]

6. Antibacterial activity

The chemically synthesized ligands and the metal complexes (1-4) had better antibacterial activity against most of the bacterial strains (Fig.) namely Staphylococcus aureus, Klebsiella pneumonia and Escherichia coli.In this study chloramphenicol is taken as the positive control. Minimal Inhibitory Concentrations of chloramphenicol against Escherchia coli and Klebsiella pneumonia is 2.0 to 3.9 µg/mL. These bacteria showed mean zone diameter of 13 to17 mm and are therefore fully susceptible to chloramphenicol. Chloramphenicol also shows good susceptibility towards Staphylococcus aureus.[38]

Table.6: Zone of inhibition (mm) against pathogenic bacteria Staphylococcus aureus.

Zone of inhibition (mm) against pathogenic bacteria (*Staphylococcusaureus)* **Concentration of metalions (µg/mL) Control-Chloramphenicol**					
S. No.	**Complex**	**3 µg/mL**	**50 µg/mL**	**75 µg/mL**	**100 µg/mL**
1	$C_{28}H_{37}N_4O_7ClCu$[1]	30.33±0.5	14.66±0.2	18.33±1.1	19.66±0.5
2	$C_{28}H_{37}N_4O_7ClNi$ [2]	29.66±0.6	15.66±0.5	18.33±0.6	24.33±0.6
3	$C_{28}H_{37}N_4O_7ClZn$[3]	30.33±0.5	13.66±0.8	16.33±0.5	18.66±0.5
4	$C_{30}H_{43}N_4O_4SV$[4]	29.66±0.5	17.33±0.5	18.66±0.0	20.00±0.0

The complex C28H37N4O7Cl Ni shows maximum activity at 100 µg/mL concentration against Staphylococcus aureus

Table 7: Zone of inhibition (mm) against pathogenic bacteria Klebsiella pneumonia.

Zone of inhibition (mm) against pathogenic bacteria (*Klebsiella pneumonia)* **Concentration of metalions (µg/mL) Control-Chloramphenicol**					
S. No.	**Complex**	**3 µg/mL**	**50 µg/mL**	**75 µg/mL**	**100 µg/mL**
1	$C_{28}H_{37}N_4O_7ClCu$[1]	23.33±0.5	10.33±0.3	12.33±0.2	14.32±0.2
2	$C_{28}H_{37}N_4O_7ClNi$ [2]	22.32±0.3	12.36±0.2	13.36±0.2	15.32±0.4

3	$C_{28}H_{37}N_4O_7ClZn$[3]	24.33±0.5	14.32±0.2	15.42±0.5	17.43±0.2
4	$C_{30}H_{43}N_4O_4SV$[4]	22.33±0.3	11.66±0.2	13.47±0.8	15.52±0.1

Zone of inhibition is highest for complex C28H37N4O7ClZn against pathogenic bacteria Klebsiella pneumonia at the highest concentration 100 µg/mL.

Table 8: Zone of inhibition (mm) against pathogenic bacteria Escherichia coli.

Zone of inhibition (mm) against pathogenic bacteria (*Escherichia coli*) Concentration of metalions (µg/mL) Control-Chloramphenicol					
S.No.	**Complex**	**3 µg/mL**	**50 µg/mL**	**75 µg/mL**	**100 µg/mL**
1	$C_{28}H_{37}N_4O_7ClCu$[1]	21.00±0.0	11.32±0.2	13.42±0.2	15.31±0.3
2	$C_{28}H_{37}N_4O_7ClNi$ [2]	22.12±0.2	12.42±0.3	14.33±0.3	16.32±0.4
3	$C_{28}H_{37}N_4O_7ClZn$[3]	21.62±0.4	13.32±0.4	14.66±0.1	16.43±0.1
4	$C_{30}H_{43}N_4O_4SV$[4]	23.32±0.3	10.33±0.2	12.32±0.5	13.44±0.2

At the concentration of 100 µg/mL, the complex C28H37N4O7ClZn has the highest zone of inhibition. The results show that the increased concentration of metal complexes exhibited maximum zone of inhibition.

Fig. 8.11 Antibacterial activity of complex.

7. Antifungal activity

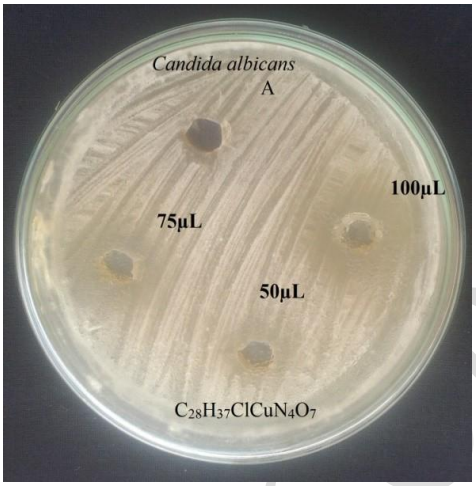
The results of antifungal activity of different concentrations of metal complexes against Aspergillus niger and Candida albicans was done by agar well diffusion method (Fig.). The results showed that the increased concentration of metal ions exhibited maximum zone of inhibition. The highest zone of inhibition was noticed against Aspergillus niger (20.02±0.1) at the concentration of 100µl for C28H37N4O7ClZn. C28H37N4O7ClNi shows Candida albicans higher zone of inhibition against 100 µg/mL concentration (17.04±0.2).[39]

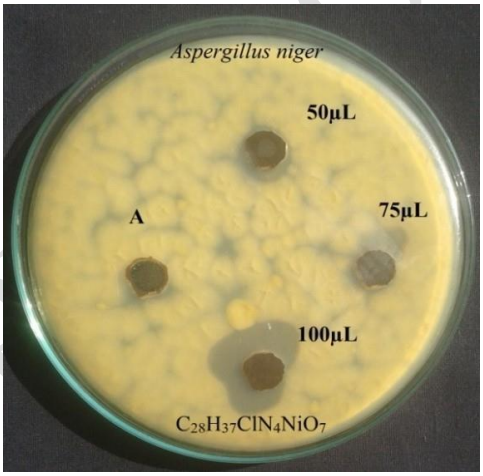
Table 9: Zone of inhibition against Aspergillus niger.

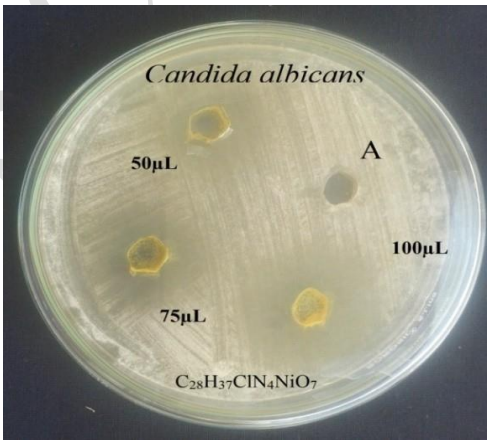
Zone of inhibition (mm) against (*Aspergillus niger*) concentration of metalions (µg/mL) Control-Fluconazole					
S.No.	**Complex**	**3 µg/mL**	**50 µg/mL**	**75 µg/mL**	**100 µg/mL**
1	$C_{28}H_{37}N_4O_7ClCu$[1]	24.02±0.3	12.01±0.2	13.06±0.1	15.03±0.3
2	$C_{28}H_{37}N_4O_7ClNi$ [2]	23.04±0.4	14.02±0.4	15.02±0.3	17.04±0.5
3	$C_{28}H_{37}N_4O_7ClZn$[3]	25.05±0.2	16.06±0.5	18.03±0.7	20.02±0.1
4	$C_{30}H_{43}N_4O_4SV$[4]	24.03±0.1	12.05±0.2	14.05±0.2	16.04±0.3

Table 10: Zone of inhibition against Candida albicans.

Zone of inhibition (mm) against (*Candida albicans*) concentration of metal ions µg/mL) Control-Fluconazole					
S.No.	**Complex**	**3 µg/mL**	**50 µg/mL**	**75 µg/mL**	**100 µg/mL**
1	$C_{28}H_{37}N_4O_7ClCu$[1]	23.04±0.3	12.01±0.4	13.00±0.4	15.02±0.5
2	$C_{28}H_{37}N_4O_7ClNi$ [2]	21.05±0.2	13.04±0.2	15.01±0.2	17.04±0.2
3	$C_{28}H_{37}N_4O_7ClZn$[3]	22.03±0.9	10.07±0.4	11.04±0.4	13.04±0.3
4	$C_{30}H_{43}N_4O_4SV$[4]	20.08±0.2	08.02±0.3	09.03±0.9	11.08±0.4







CONCLUSION

The present study provides information in respect of The metal complexes were synthesized using the backbone of Schiff base ligands and characterized using spectral techniques like UV-Vis, FT-IR. One of the ligand was isolated in crystal forms which give the exact structure of the particular compound and additionally supports the formation of metal complexes using the moiety. The spectrum of the copper complexes explains the paramagnetic nature. The cyclic voltammogram supports the various oxidation and reduction state of synthesized copper complexes.

Details on the biological studies of the synthesized three ligands and twelve metal complexes are presented in the thesis. The structures are confirmed by various spectral methods. The molecular docking study supports the binding nature of the synthesized complexes with biomolecule. The antifungal and antibacterial result of the metal complexes explains such compounds acts like

potential anti infection drugs. The mosquitocidal studies support the compounds resembles the anti-dengue drugs. The synthesized metal complexes interacted with DA6, DA17, DG4, DG22, DG23, DA5, DT19, DG4, DG16, DT7, DC21, DC24 and DT8 nucleotide of the DNA molecule. According to the binding energy values the order of best three compounds towards DNA molecules are 3 > 9 > 11. So many amino acid residues were involves in the binding study.

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