Tuijin Jishu/Journal of Propulsion Technology
ISSN: 1001-4055
Vol. 47 No. 03 (2026)

Molecular Docking and Biological Evaluation of Synthesized Compounds for Prospective Biomedical Applications

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Abstract:- A novel Schiff base ligand was obtained by the reaction of p-anisidine (4-methoxy aniline) and 3-ethoxy salicylaldehyde (3-ethoxy-2-hydroxy benzaldehyde) and their complexes with the metal Ni $^{++}$ and Zn $^{++}$ were obtained. Characterization of the ligand and metal complexes were done by elemental analysis, molar conductance and magnetic susceptibility measurements and spectroscopies methods.

Furthermore, the in vitro & in silico activity of the ligand and its metal complexes was assessed by different biological assays. The results of the study show that the binding energies are (-96.9 -110.09 kcal/mol) in trypsin activity. Among them, 5(c) compound had the least energy values, which suggests the most stable binding. In the process of pepsin docking, the binding energies are -67.9 to -73.4 kcal/mol, 5(b) having the best binding ability. In the case of lipase, the binding energy of compounds is -77.5 to -99.115 kcal/mol, where 5(c) exhibited the best affinity. The docking results shows good binding energies together with the establishment of strong intermolecular interactions, such as hydrogen bonding and hydrophobic contacts, which comprise the main features of enzyme ligand binding. The results of these computations study (Insilco) show a good correlation with the in-vitro laboratory results.

Keywords: Schiff base, Ligands-Metal Complexes, Anti enzymatic, Characterization Molecular docking.

1. Introduction

Organic reaction refers to condensation of two or more molecules to give new compounds which have specific biological behaviors. These reactions are commonly employed in the design of drugs (1). The synthesis of Schiff bases is due to condensation reactions that occur between primary amines and ketones or aldehydes which are formed under certain conditions. Due to their various industrial and catalytic applications, broad spectrum of biological activities, and ability to stabilize metal ions in different oxidation states, Schiff bases have attained a great significance (2, 3). The formation of nitrogen bond with metals provides a stable complex since after bonding, the nitrogen atom has a lone pair of electrons on the imine linkage (N=CH) (4, 5). These stable complexes, which have profound influence on bio-inorganic, supramolecular chemistry, molecular magnetism, and various vital biological processes, have garnered a lot of attention (6, 7). Besides having an antibacterial antiviral, antifungal and antienzymatic activity, imine complexes possess a wide range of biological properties (8). Moreover, they might be also applied in enzyme immobilization (9, 10).

The digestive enzymes are proteins which play a major role in the process of digestion. They promote to break down complex food molecules to simple and more absorbable forms to be used in the energy production and other

processes. Some of the enzymes like amylase, trypsin, lipase, and pepsin are vital in facilitating the digestion of different macronutrients in the body. Proteases are very important in the process of decomposing proteins in order to separate them into amino acids. One endocrine system related chronic syndrome is diabetes mellitus caused by the conversion of starch to sugars by amylases and lipids to fatty acids and glycerol by lipases (11-13). It has an influence on both metabolism and various components such as water, electrolytes, fats, proteins and carbs (14). Hyperglycaemia is the main characteristic of diabetes induced by a deficiency in insulin secretion or insulin-insensitive cells that are unable to break down 1,4-glycosidic bond of carbohydrates into smaller molecules, e.g., starch into glucose, and is involved in their digestion. α-Amylase is a metalloenzyme digesting 1,4-gly There are a number of health conditions associated with high levels of blood glucose such as diabetes, obesity, and dental diseases (15). Some of the medical conditions caused by diabetes include nephropathy, microangiopathy, neuropathy, retinopathy and cardiovascular diseases. Hence, one of the potential targets of lead molecules in the management of diabetes is the inhibitors of α-amylase (16).

One of the new and widespread health problems is obesity. Human health may suffer greatly as a result of the increased body fat. Based on WHO statistics, one of the primary causes of cancer sickness is obesity. One of the enzymes, trypsin, plays a vital role in the digestive system and helps to break down food protein to peptide and amino acid. Small intestine has the enzyme trypsin, which is a serine protease that assists in protein breakdown. An anti-inflammatory and tissue-repair promoter, this proteolytic enzyme finds widespread application. Nevertheless, activation of trypsin may be very important but can damage some cells leading to pancreatitis when it is beyond a certain point. There is the need to regulate the activity of trypsin therefore. Pepsin is a protease enzyme, precipitated by low pH of 1.5-2 and helps the stomach to digest complex proteins. An increased amount of pepsin is liberated as the stomach becomes more acidic and therefore, leads to ingestion of the stomach lining. This may lead to inflammation of the surrounding tissues that may cause ear infections, polyps of the vocal folds, enlarged tonsils among a host of other diseases. Thus, the goal will be to produce and investigate the activity of the novel compounds on digestive enzymes like trypsin, amylase, lipase, and pepsin. To determine the antinutritional effects, the effect of amylase, trypsin, pepsin and lipase is essential. Computational techniques have become a significant tool in the last few years in the process of discovering and developing new drugs. These Computational methods enhance the effectiveness and accuracy of the identification of good candidate with improved biological activities (17-18).

In addition, the in vitro and in silico antienzymatic activities of the ligand, and the metal complexes were investigated using various biological assays. (19-21).

2. Materials & Methodology

A chemical synthesis of the Schiff base and its transition metal complexes was done using chemicals, reagents, and solvents of analytical quality, which were bought at Sigma Aldrich.

The samples were referred to SAIF Chandigarh and Cochin to carry out the FTIR, UV spectral characterization and CHN elemental characterization.

Synthesis of Ligands& Preparation of Metal Complex

The Schiff base ligand was prepared due to condensing 3- Ethoxy salicylaldehyde with P- Anisidine. About 20 ml of 0.05 mol ethanolic solution of 3-Ethoxysalicylaldehyde and 0.05 mol of P-Anisidine in an ethyl alcohol solution were put together and stirred at a speed of 300- 400 rpm at room temperature using a magnetic stirrer. This yellow solid is subsequently filtered and dried in oven at 100^{o}C. Recrystallization is done in ethyl alcohol and purified with diethyl ether. Crystallized Complex putted into a desiccator containing anhydrous calcium hydroxide in order to dry the synthesized ligand & Complex. The prepared ligand was, in turn, used to further synthesis of metal complexes (22-23). Transition metal complexes (Zn^{+2} and Ni^{+2}) by mixing the solutions of metal salts (0.005mol) in a minimum quantity of water with the solution of ligand (0.005mol) in 20 ml DMSO, stirring for 4- 5 hrs. on the magnetic stirrer at 300- 400 rpm, followed by filtration under suction on Whatman filter paper washing with distilled water, then alcohol, dried and recrystallized in DMF. Fig:1 (24)

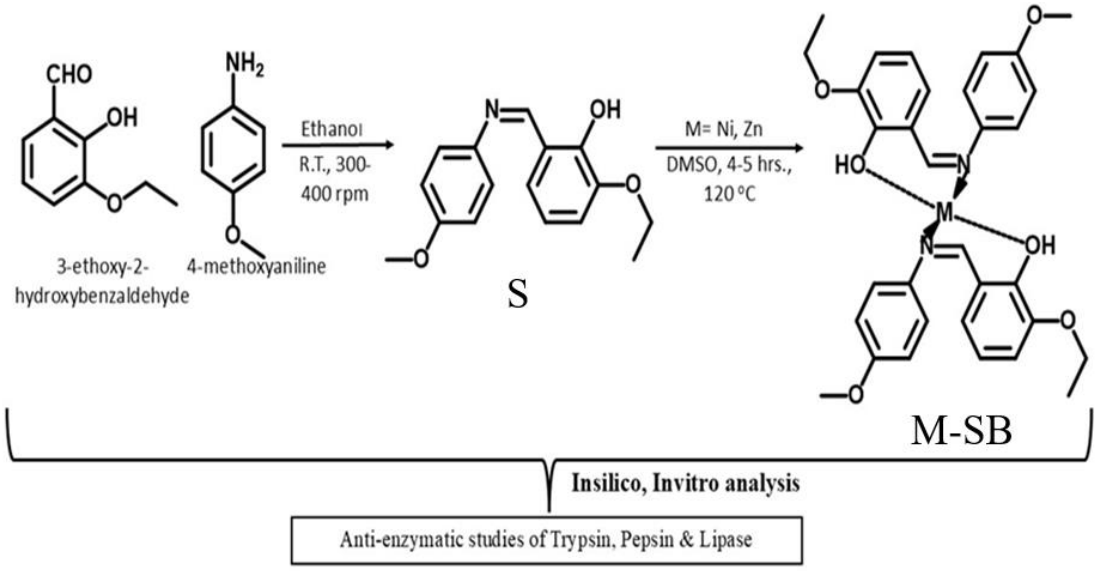


Figure 1

3. Characterization

Elemental Analysis

CHN elemental analysis was carried out on the Schiff base ligand and its transition metal complexes by SAIF Chandigarh and Cochin Table (1). The results agree well with those calculated for the proposed ligand and metal complex structures (25). Results of Physical Properties are reported in Table (2).

Table 1. Elemental analysis of ligand and metal complexes

Ligand/ Complex	C (%)		H (%)		N (%)	
	Cal.	Found	Cal.	Found	Cal.	Found
5(a) : SBL-I	70.77	69.54	6.27	6.28	5.16	5.34
5(b) : Ni^{2+}-SBL-I Complex	64.06	64.21	5.33	5.41	4.67	5.15
5(c) : Zn^{2+}-SBL-I Complex	63.36	63.48	5.28	5.36	4.67	4.78

Table 2. Physical properties color, melting point, percentage yield and molar conductance of ligand and metal complexes

Ligand/ Complex	Color	Melting point ($\pm 2^0$C)	% yield	Molar conductance ($ohm^{-2}cm^2mol^{-1}$
5(a) : SBL-I	Light Brown	189	75	-
5(b) : Ni^{2+}-SBL-I Complex	Yellow Brown	220	70	55
5(c) : Zn^{2+}-SBL-I Complex	Yellow	245	65	55

Measurement of Magnetic Susceptibility

The values are illustrated in Table 3. Based on the results, the metal complexes are found to be non, electrolytic. The values of the molar conductance are used to indicate the ratio of the metal and the ligand of 1:2. Among all the metal complexes Ni^{+2} metal complexes are diamagnetic whereas Zn^{+2} is paramagnetic in nature. Table (3).

Table 3. Magnetic & UV-Visible

Ligand/Complex	μ_{eff} (B.M.)		λ_{max} (nm)
	Theoretical	Experimental	
5(a) : SBL-I	-	-	230 nm – 275 nm
5(b) : Ni^{2+}-SBL-I Complex	1.78	1.74 (paramagnetic)	360 nm – 420 nm
5(c) : Zn^{2+}-SBL-I Complex	1.78	1.75 (Diamagnetic)	380 nm – 450 nm

FTIR Characterization of Ligand & Complexes

FTIR spectrum of Schiff ligand reveals the absence of IR peaks corresponding to primary amine group (NH_2) and carbonyl group (CHO) from aldehyde. A peak is observed at 1170-1055 cm^{-1} stretching due to C-O-C of methoxy &ethoxy. The presence of the band at 1650 cm^{-1} confirms the formation of azomethine linkage between primary amine and aldehyde which occurred through condensation resulting in the formation of Schiff base from primary amine and aldehyde. The IR peak observed at 1650 cm^{-1} confirms the formation of imine linkage between primary amine and aldehyde which occurred through condensation resulting in the formation of Schiff base from primary amine and aldehyde (26-27). The IR peak observed in the 3350, 3328 cm^{-1} region is due to (NH). The band at 1450 cm^{-1} to (C-N) Fig (2). The disappearance of the phenolic –OH band and appearance of new M–O and M–N bands supported bidentate coordination.

X-Ray Diffraction Studies:

The X, ray diffraction pattern of Ligand is illustrated in Fig (3). The pattern of XRD of the Schiff base ligand is characterized by the well-defined crystalline peaks and it implies that the ligand sample was in the crystalline form Fig (3). Crystalline reflections are confirmed by the four sharp peaks at the following angles: 14, 17, 22, and 24 (29).

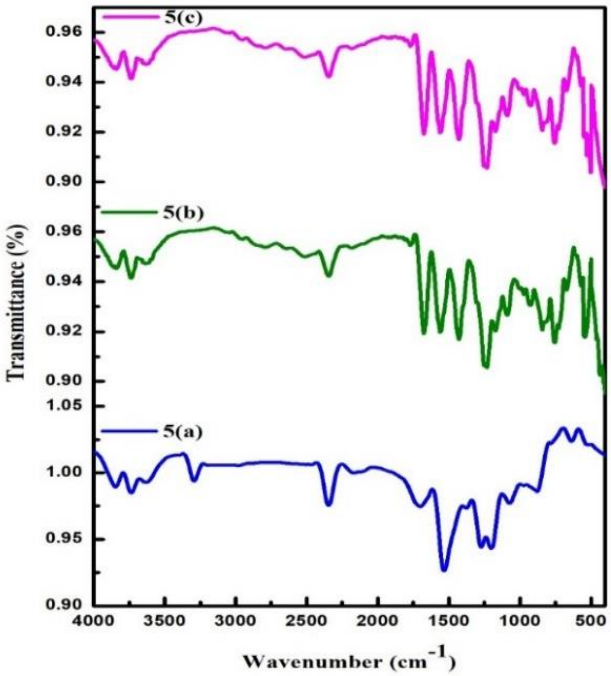


Figure 2. FTIR (Ligand & Metal Complex)

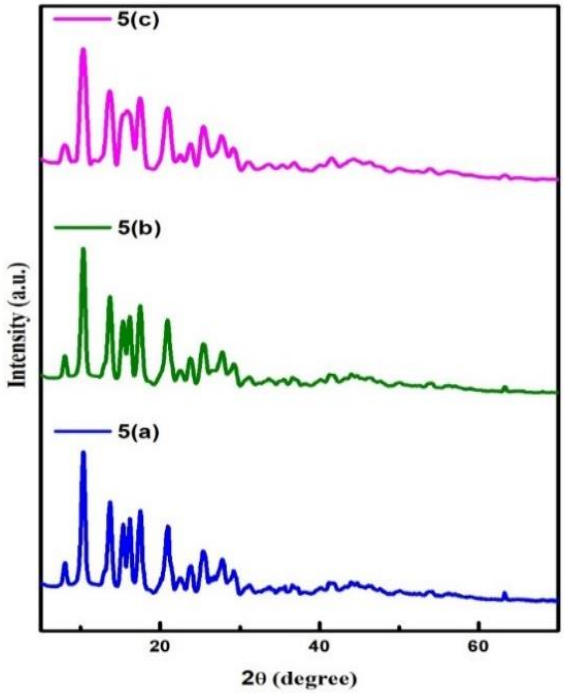


Figure 3. XRD (Ligand & Metal Complex)

Electronic Spectra:

Measurement of the electronic spectra at room temperature was done in the DMSO solution ranging between 200 and 800 nm of the ligand and complexes. The free Schiff base ligand has yielded two absorption bands in the UV-Vis spectra at 230 and 299 nm that are attributed to 230 and 299 nm respectively. n- π * transitions, respectively. Complexes Two charge transfer (C.T.) peaks appear in complexes UV-Vis spectra. The electronic spectra of the ligand and complexes show two absorption bands at 319 nm and 416 nm. The higher intensity band of the first band is attributed to ligand metal charge transfer transition (28). Results are reported in table (3).

Scanning Electron Microscopy (SEM) Analysis

Scanning electron microscopy was used to study the surface morphologies of new Schiff base transition metal complexes. SEM images of Zn and Ni complexes are shown as Fig. (4) These complexes have leaflet and amorphous surface morphologies and are micro sized. The synthesized transition metal complex (30-31)

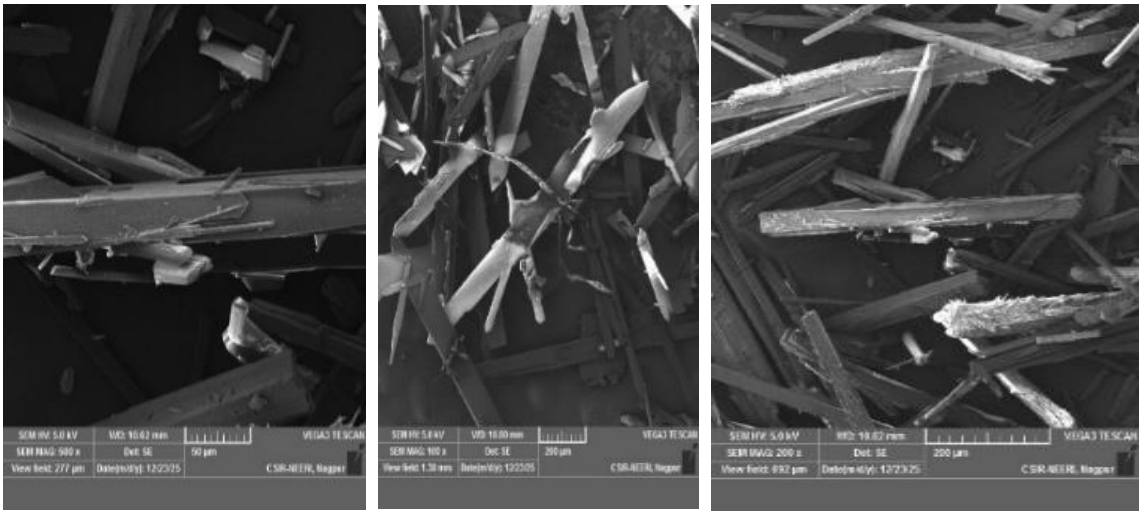


Figure 4 & 5

4. Antimicrobial Activity

New Schiff-base ligands and their transition metal (Zn, Ni) complexes were initially studied on two fungi and two bacteria: Aspergillus Niger and Candida albicans; Gram negative Escherichia coli and Gram, positive Staphylococcus aureus, respectively. (32-34).Agar disc diffusion procedure was performed and compared with the known Streptomycin to screen antibacterial activity with ligands that were dissolved in either DMSO solvent or DMF solvent and the concentration of the ligands was 100 ppm as indicated in table Table (4) &Fig (5).The obtained anti and microbial screening results indicate that, the Schiff base and the transition metal (Zn, Ni) complexes of the Schiff base possess moderate antibacterial actions .

Table 4. Anti-microbial screening values of Schiff base ligand and its transition metal complexes

Anti-microbial Screening of Schiff base ligand and their transition metal, Ni (II)& Zn (II) complexes				
Ligand/Complex	Zone of Inhibition(mm)			
	Antibacterial Screening		Antifungal Screening	
	E. Coli	S. Auresus	A. Niger	C. Albicans
5(a): SBL[$C_{16}H_{17}NO_3$]	13.5	15	---	---
5(b) : Zn[$C_{32}H_{32}N_2O_6$]	8	6	---	4
5(c) : Ni[$C_{32}H_{32}N_2O_6$]	6	5	---	---

Anti-Enzymatic Study This was done on the action of synthetic ligands and their transition metal on the digestive enzymes, pepsin, trypsin and lipase. The results have been reported in table (5) &Fig (6)

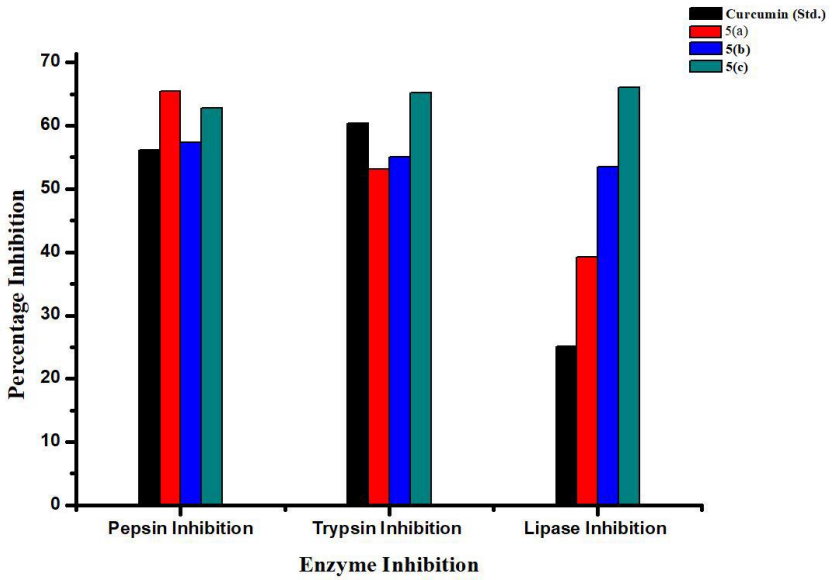


Figure 6. Antienzymatic Study of ligand & metal complexes

5. Molecular Docking

The binding affinity obtained from iGemdock reveals the interaction between the ligand and the protein molecule. The enzymes demonstrated proper positioning of their catalytic residues, essential for converting reactants into products. All docking experiments were conducted through where active site of both ligands and the enzyme had to be in a specific format. The structure of α-amylase, lipase, trypsin and pepsin were retrieved from Protein Data Bank (38-39).

The docking analysis indicates that the Schiff base formed by 3-ethoxy salicylaldehyde and p-anisidine can easily be placed in the enzyme active site. The enzymes were found to have the right orientation of their catalytic residues which are necessary in the conversion of the reactants to produce products. In the case of trypsin, the active site amino acids are Ser195, His57 and Asp102, in lipase, Ser152, Asp176 and His263 and in pepsin, Asp 32, Asp 215(18). The summation of the energy, Van der Waals (VDW), hydrogen bonding (HB), electrostatic energy is discussed in Table no (6) & Fig (7).

Table 6. Total energy of all compounds by using *in-silico* studies

Enzyme	Compound	Energy Kcal/mol	Vanderwall interaction	H-bonding interaction	Total no. of interaction	Hydrogen bonding interaction	Hydrophobic interaction	other
Trypsin	5a: SBL-I	-96.91	-76.8	-20.1	9	4	4	1
	5b: Ni^{2+}-SBL-I Complex	-108.93	-91.69	-17.23	7	5	1	1
	5c: Zn^{2+}-SBL-I Complex	-110.09	-104.02	-6.06	9	2	7	0
Pepsin	5a: SBL-I	-77.5	-62.27	-15.22	8	7	1	0
	5b :Ni^{2+}SBL-I Complex	-99.315	-79.82	-19.48	4	1	3	0
	5c: Zn^{2+}-SBL-I Complex	-86.433	-72.33	-14.0	5	2	3	0
Lipase	5a :SBL-I	-72.302	-60.07	-12.2	7	2	5	0
	5b: Ni^{2+}-SBL-I Complex	-67.904	-57.59	-10.31	13	0	11	2
	5c: Zn^{2+}-SBL-I Complex	-73.04	-69.54	-3.5	18	0	17	1

In Silico Study of Metal Complexes & Ligands

This ligand was highly specific to trypsin, pepsin, Lipase and a number of hydrogen and hydrophobic bonds were established in the active sites of the two suggesting that this ligand was able to block the entry-point of the substrates. When it comes to Trypsin, Pepsin and lipase, the ligand was found to develop moderate to good binding which was stabilized by hydrophobic contacts and van der Waals forces with limited hydrogen bonds. The in-silico observations were quite consistent with its predicted antienzymatic activity (40-42).

The 3-ethoxysalicylaldehyde-para-anisidine Schiff base complexes of Zn (II) and Ni (II) with digestive enzymes (trypsin, pepsin and lipase) were conducted in molecular docking. Furthermore, the in vitro & in silico antienzymatic activity of the ligand and its metal complexes was assessed by different biological assays. The results of the bioassay shows that the binding energies (-96.9 to -110.09 kcal/mol) in trypsin inhibition were between (-96.9 to -110.09 kcal/mol). Compound 5(c) exhibited the smallest energy values among them, which is the most stable binding. The energies of compounds in lipase docking were all within the range of -67.904 to -73.4kcal/mol with 5(c) exhibiting the most binding affinity. The binding energies of compounds of pepsin were -77.5 to -99.115 kcal/mol Compound 5(b) exhibiting the highest binding affinity.

The docking results showed good binding energies together with the establishment of strong intermolecular interactions, such as hydrogen bonding and hydrophobic contacts, which comprise the main features of enzyme ligand binding. These computational results have a good correlation with the laboratory in vitro data. The

combined in vitro& in silico studies reveal that the novel Schiff base transition metal complexes have a good biological potential. (43-45)

Total binding energies of both metal complexes were negative and displayed strong and stable interactions involving enzymes and metal complexes in Fig (7)

6. Conclusion

We have been able to design and synthesize in this research a novel series of 3-ethoxy salicylaldehyde Para anisidine ligands and its complexes (5b and 5c). Bidentate coordination and stable complex formation were confirmed by spectral studies. The synthesized compounds were all tested on their Microbial activity against bacteria as well as against enzymes like the pepsin, trypsin and lipase enzymes. Most of the compounds that were synthesized showed great concentration of enzyme-inhibitory activity. Moreover, the compounds in molecular docking studies showed improved binding to the target site. The compounds 5a, 5b and 5c have shown good inhibitory capacity (46) with pepsin, trypsin and lipase. These computational results have a good correlation with the laboratory in vitro data. The combined in vitro& in silico studies reveal that the novel Schiff base transition metal complexes have a good biological potential.

The development of new lead in developing drugs against many pathological disorders at which these enzymes are involved is expected to be given by these studies.

Acknowledgement

Authors of this paper are very much thankful to the RTMNU, IIL, Nagpur & Director of Institute of Science, Nagpur for providing the infrastructural support. We are also thankful to SAIF Chandigarh and Cochin for providing the spectral analysis of Schiff base ligand and its complexes.

Conflict of Interest

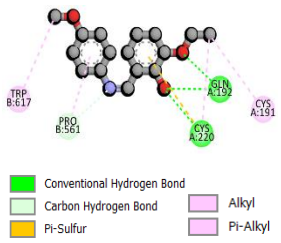
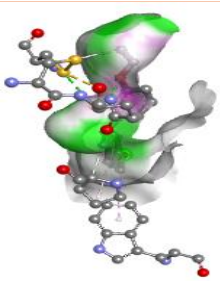
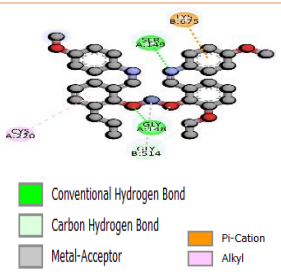
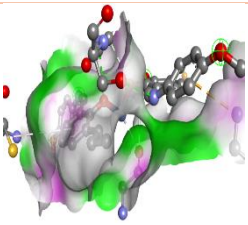
Authors of this paper do not have any conflict of interest.

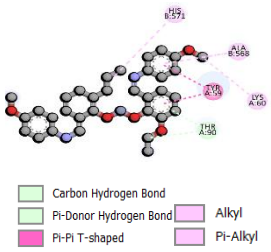
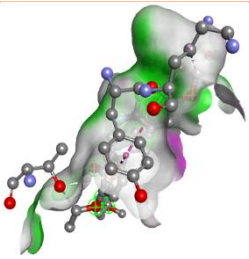
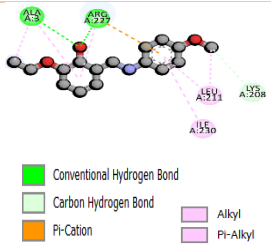
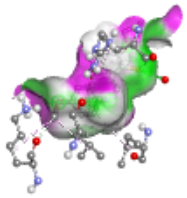
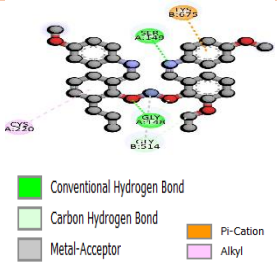
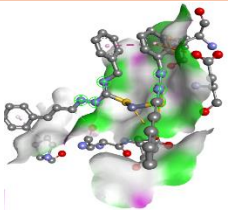
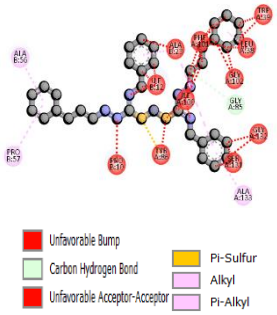
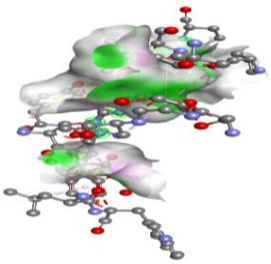
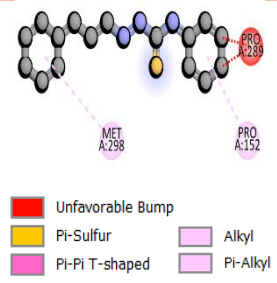
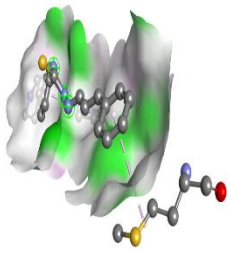
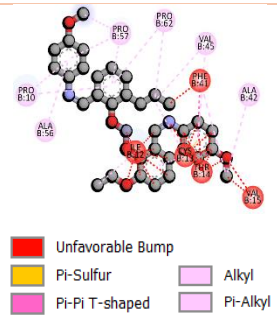
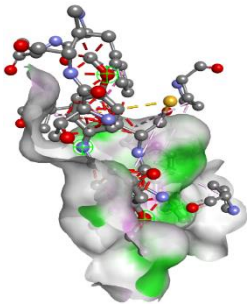
Funding

Rajiv Gandhi Science &Technology Commission & RTMNU, Nagpur for Financial Support.

Data Availability Statement

The data of this research is included in this published article and its supplementary files. Additional data are available from the corresponding author on request.

Trypsin:5(a) : SBL-I		
Trypsin: 5(b) : Ni^{2+}-SBL-I Complex		

Trypsin:5(c) : Zn^{2+}-SBL-I Complex		
Pepsin: 5(a) : SBL-I		
Pepsin :5(b) Ni^{2+}-SBL-I Complex		
Pepsin :5(c) Zn^{2+}-SBL-I Complex		
Lipase:5(a) : SBL-I		
Lipase :5(b) Ni^{2+}-SBL-I Complex		

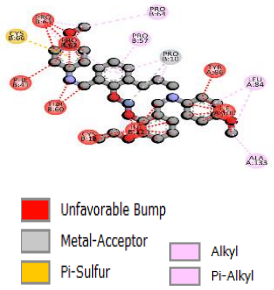
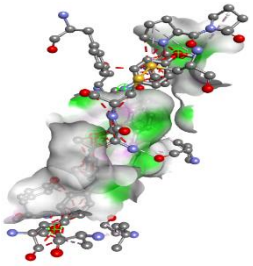
Lipase:5(c) : Zn^{2+}-SBL-I Complex		

Figure 7. Docking images of all compounds

References

[1] Abbas, Mohammed N., Dhuha S. Ahmed, and Akram A. Al-Amiery. "Synthesis and spectroscopic characterization of Schiff base metal complexes, biological activity, and molecular docking studies." ACS Omega, 2024, vol.9, no. 6, pp. 5401–5412. https://doi.org/10.1021/acsomega.3c08526

[2] Mahmood, Zaffar, et al. "Recent advances in biological and medicinal profile of Schiff bases and their metal complexes: An updated version (2018–2023)." Journal of Saudi Chemical Society, 2023,vol. 27, no. 4, article 101726. **https://doi.org/10.1016/j.jscs.2023.101726**

[3] Ganesan Venkatesh etal ACS omega biological screening and spectroscopic investigation of biologically active Schiff base transition metal complexes 2024,9,8123−8138 https://pubs.acs.org/doi/10.1021/acsomega.3c08526

[4] Rajput, S. J., and D. R. Shah. "Biological evaluation and molecular docking of Schiff base metal complexes derived from aromatic aldehydes." Medicinal Chemistry Research, 2020, vol. 29, no. 9, pp. 1524–1535. doi: 10.1007/s00044-020-02581-2

[5] Shahabadi, Nahid, Lida Heidari, and Saeid Kashanian. "DNA-binding and antimicrobial studies of a new Schiff base and its Ni (II) complex." Spectrochemical Acta Part A: Molecular and Biomolecular Spectroscopy,2019 vol. 206, pp. 423–429.

[6] Deepa, M., and R. Ramesh. "Synthesis, characterization, antimicrobial, DNA binding and cleavage studies of Schiff base Cu (II), Ni (II) and Zn (II) complexes." Journal of Molecular Structure, vol.2018 1166, pp. 234–243.

[7] Sadeek, S. A., W. H. El-Shwiniy, and W. A. Zordok. "Synthesis, characterization, and biological studies of Schiff base metal complexes of 3-methoxysalicylaldehyde." Journal of Molecular Liquids2019, vol. 275, pp. 888–900.

[8] Yadav M etal Designing, spectroscopic characterization, biological screening and antioxidant activity of mononuclear transition metal complexes of bidentate Schiff base hydrazones J. Chem. Sci. (2021) 133:21 https://doi.org/10.1007/s12039-020-01854-6

[9] B. Nandini Metal Complexes with Schiff Bases - A Review of their Antimicrobial Activities Current Bioactive Compounds August 2024 21,5,224-245 DOI:10.2174/0115734072305971240816114116

[10] Kaur, P., Berar, U., & Raghav, N. Exploring digestive enzymes' differential affectivity of synthesized 2-thienyl-based chalcones. Future. Med. Chem. 2025; 1-11. https://doi.org/10.1080/17568919.2025.2527583

[11] Salam M A, Affan MA, Ahmad FB and Arafath MDA 2012 Organotin (IV) complexes with pyruvic acid phenylhydrazone (HPAPD): synthesis, spectral characterization, and in vitro antibacterial activity J. Coord. Chem. 2012,65 1999.

[12] Petya Emilova Marinova* and Kristina Dimova Tamahkyarova Synthesis, Investigation, Biological Evaluation, and Application of Coordination Compounds with Schiff Base—A Review Compounds **2025**, *5*(2),14; https://doi.org/10.3390/compounds5020014

[13] Kaur P, Raghav N, Sharma P. K, & Ram S. Development of benzene sulfonamide containing 1, 2, 3-triazole and 1, 3, 4-oxadiazole hybrids as cathepsin B inhibitors and DFT calculations. J. Mol. Struct. 2025; 1320, 139680. https://doi.org/10.1016/j.molstruc.2024.139680.

[14] Kaur P, Raghav N, & Berar U. Multi-targeted Thiophene Based Effective Digestive Enzyme Inhibitors: Synthesis and Enzyme Inhibition Studies. J. Mol. Struct. 2025; 141748. https://doi.org/10.1016/j.molstruc.2025.141748.
[15] Monika, Chander, Kaur P, Raghav N, Sharma PK, et al. Synthesis, Biological Evaluation, and Computational Studies of Schiff's Base Derivatives of 4-(4-Amino-5-Mercapto-4H-1, 2, 4-Triazol-3-Yl) Benzenesulfonamide as Cathepsin B Inhibitors. Chem. Biodiversity. 2025: e202402575. https://doi.org/10.1002/cbdv.202402575.
[16] Panel Naol Mohammed etal Synthesis, molecular docking Studies, and evaluation of antibacterial and antioxidant activities of pyrazoline derivative June 2024, vol(8) 101570,1-9 https://doi.org/10.1016/j.rechem.2024.101570
[17] David O Oladejo etal in silico Structure Prediction, Molecular Docking, and Dynamic Simulation of Plasmodium falciparum Bioinformatics and Biology Insights Jan 23,2023 https://doi.org/10.1177/11779322221149616
[18] Suresh, P. S., Kumar, A., Kumar, R. & Singh, V. P. An in-silico approach to bioremediation: Laccase as a case study. J. Mol. Graph Model 2008,26(5), 845.9. 10.1016/j.jmgm.2007.05.005
[19] Gaba, M., Gaba, P., Singh, S. & Gupta, G. D. An overview of molecular docking. Int. J. Drug Dev. Res. 2010, 2(2), 219-231
[20] Pedro H M Torres , Ana C R Sodero , Paula Jofily , Floriano P Silva-Jr Key Topics in Molecular Docking for Drug Design Int J Mol Sci 2019 Sep 15;20(18):4574**. 10.3390/ijms20184574**
[21] Leonardo G. Ferreira, Ricardo N. Dos Santos, Glaucius Oliva Molecular Docking and Structure-Based Drug Design Strategies Molecules2015, 20(7), 13384-13421, https://doi.org/10.3390/molecules200713384
[22] Krishna R. Gupta etal Insights into molecular docking: A comprehensive view International Journal of Pharmaceutical Chemistry and Analysis. 2023,10(3):175-184 https://doi.org/10.18231/j.ijpca.2023.030
[23] Marshall GR Computer Aided Drug Design. Annual Review of Pharmacology and Toxicology,1987, 01,27:193-213. https://doi.org/10.1146/annurev.pa.27.040187.001205
[24] Singh K., Agarwala B.V. Structural study of lanthanide complexes formed with o-Vanillin sallicyloylhydrozone and o-vaniilin p-anisidine "Spectroscopy letter" 1995,28(3) 747-760 https://doi.org/10.1080/00387019508009916
[25] Agarwal A, V Chanchal, Raghav N Deasin, Synthesis &Molecular Docking studies of 123 new Triazole linked nucleobases" Results in Chemistry" 13,2025,10 2011 https://doi.org/10.1016/j.rechem.2024.102011
[26] Aimad, A., Sanae, R., Mostafa, S., Dalal, M., Noureddine, E., and Mohamed, F. (2021). Gc-MS analysis of essential oil composition and insecticidal activity of syzygium aromaticum against callosobruchus maculatus of chickpea. Trop. J. Nat. Prod. Res. 5, 844–849. doi:10.26538/tjnpr/v5i5.9
[27] Chebbac, K., Ghneim, H. K., El Moussaoui, A., Bourhia, M., El Barnossi, A., Benziane Ouaritini, Z., et al. Antioxidant and antimicrobial activities of chemically-characterized essential oil from Artemisia aragonensis Lam. against drug-resistant microbes. Molecules 2022,27, 1136. 10.3390/molecules27031136
[28] Biala G, Kedzierska E, Kruk-Slomka M, Orzelska-Gorka J, Hmaidan S, Skrok A, Kaminski J, Havrankova E, Nadaska D, Malik I. Research in the Field of Drug Design and Development. Pharmaceuticals (Basel). 2023 Sep 11;16(9):1283. doi: 10.3390/ph16091283. PMID: 37765091; PMCID: PMC10536713.
[29] Singh N, Vayer P, Tanwar S, Poyet J-L, Tsaioun K and Villoutreix BO (2023) Drug discovery and development: introduction to the general public and patient groups. Front. Drug Discovery. 3:1201419. doi: 10.3389/fddsv.2023.1201419
[30] Eno, E. A., Mbonu, J. I., Louis, H., Patrick-Inezi, F. S., Gber, T. E., Unimuke, T. O., et al. (2022). Antimicrobial activities of 1-phenyl-3-methyl-4-trichloroacetyl-pyrazolone: Experimental, DFT studies, and molecular docking investigation. J. Indian Chem. Soc. 99, 100524. https://doi.org/10.1016/j.jics.2022.100524
[31] Kausar Shaheen Synthesis, Characterization, and Multifunctional Applications of Cu-Fe and Ni-Fe Nanomaterials ACS Omega June 23, 2020 Vol 5/Issue 26 .https://pubs.acs.org/doi/10.1021/acsomega.0c01259

[32] Biala G, Kedzierska E, Kruk-Slomka M, Orzelska-Gorka J, Hmaidan S, Skrok A, Kaminski J, Havrankova E, Nadaska D, Malik I. Research in the Field of Drug Design and Development. Pharmaceuticals (Basel). 2023 Sep 11;16(9):1283. doi: 10.3390/ph16091283. PMID: 37765091; PMCID: PMC10536713.
[33] lharbi, N. S., Alsubhi, N. S. & Felimban, A. I. Green synthesis of silver nanoparticles using medicinal plants: Characterization and application. J. Radiat. Res. Appl. Sci. 2022,**15**(3), 109–124. https://doi.org/10.1016/j.jrras.2022.06.012 .
[34] MuhammadImranDin Volume 50, 2017 - Issue 1 Synthesis, Characterization, and Applications of Copper Nanoparticles https://doi.org/10.1080/00032719.2016.1172081
[35] Hamed Ghanbari, Scientific Reports)Synthesis, characterization, and biological activity of a fresh class of Sono chemically synthesized Cu^{2+} complexes volume 14, Article number: 2024,21325
[36] Jain R. Review on Computational Bioinformatics and Molecular Modelling: Novel Tool for Drug Discovery. Int J Trend Sci Res Dev . 2018;3(1):1-56
[37] Gschwend DA, Good AC, Kuntz ID. Molecular docking towards drug discovery. J Mol Recognin. 1996;9(2):175-86. https://doi.org/10.1002/(SICI)1099-1352(199603)9:2<
[38] Rarey M, Kramer B, Lengauer T, Klebe G. A fast flexible docking method using an incremental construction algorithm. J Mol Biol. 1996;261(3):470-89 https://doi.org/10.1006/jmbi.1996.0477
[39] Kitchen D, Decornez H, Furr J, Bajorath J. Docking and scoring in virtual screening for drug discovery: methods and applications. Nat Rev Drug Discov. 2004;3(11):935-84
[40] Venkatachalam CM, Jiang X, Oldfield T, Waldman M. Ligand Fit: a novel method for the shape-directed rapid docking of ligands to protein active sites. J Mol Graph Model. 2003;21(4):289-307 https://doi.org/10.1016/S1093-3263(02)00164-X
[41] Safaa Rhaimi, Mohamed Taibi, Molecular Docking Analysis, Chemical Composition, and Evaluation of Antibacterial and Insecticidal Activity of *Salvia officinalis* Essential Oil Journal of Food Processing and Preservation Volume 2024, Article ID 9961973, 13 **https://doi.org/10.1155/jfpp/9961973Digital Object Identifier (DOI)**
[42] Agour, A, Mssillou I. et al., “Pharmacological activi-ties of chemically characterized essential oils from Haplophyl-lum tuberculatum (Forssk.),” Frontiers in Chemistry, 2023, vol. 11, article 1251449, 2023. https://doi.org/10.3389/fchem.2023.1251449
[43] Agarwal A, V Chanchal, Raghav N Deasin, Synthesis &Molecular Docking studies of 123 new Triazole linked nucleobases” Results in Chemistry” 13, (2025),10 2011 https://doi.org/10.1016/j.rechem.2024.102011
[44] Luca Pinzi* Molecular Docking: Shifting Paradigms in Drug Discovery International Journal of Molecular Sciences 2019, *20*(18), 4331;https://doi.org/10.3390/ijms20184331
[45] Jain, A.N. Effects of protein conformation in docking: improved pose prediction through protein pocket adaptation. J. Comput. Aided. Mol. Des. **2009**, *23*, 355–374 DOI:10.1007/s10822-009-9266-3
[46] Vashisth C, & Raghav N. Preferential inhibition of α-amylase by cinnamaldehyde-based hydrazones: A comparative study. Int. J. Biol. Macromol. 2024; 281: 136654. https://doi.org/10.1016/j.ijbiomac.2024.136654