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Original Article

Developing New Organometal Complexes of Schiff Base Derivatives with Anticancer Potentials

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ABSTRACT

Organometallic compounds are gaining prominence today as they are found to be potent anticancer agents due to their diverse chemical nature along with the metal with which they are chelated. In these organometallic compounds, many different hetero-organic compounds like Schiff bases, Indoles, Quinolines, Pyrroles are chelated with different metals. As these heterocyclic compounds are proven cytotoxic agents at a higher dose, their potency get enhanced by many fold by metal complexation. Schiff base derivatives are reportedly more powerful agents against tumours of different types, they are gaining prominence as antitumour agents. In this present study, different derivatives of Schiff bases are synthesized and chelated with Aluminium (Al) and characterised with IR, NMR, LCMS and also subjected to metal analysis by ICPMS. Later, these compounds were screened by *in vitro* analysis of their cytotoxic potentials against cancer cell lines by MCF method and are found to be potent cytotoxic agents. Among all, MC-2 and MC-3 are nearer to the cytotoxic range given by NIH. Hence, we anticipate that although all the synthesized organometal complexes are potential cytotoxic agents, however MC 1 and MC 5 are significantly good cytotoxic agents. However, further study is needed to justify this claim.

Keywords: Organometallic compounds, Metal chelates, Schiff base derivatives, Anticancer agents, and Antitumour agents.

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INTRODUCTION

In 1930, the landscape of medicinal chemistry underwent a transformative shift, fostering the synthesis and advancement of numerous synthetic drugs. Until that point, drug research predominantly centered on natural products. However, in contemporary times, the spectrum of diseases treatable with synthetic drugs has expanded significantly. Consequently, there is a pressing need to innovate techniques for the synthesis and purification of diverse bioactive compounds. The advent of target-based drug design was achieved through a comprehensive exploration of Structure-Activity Relationship (SAR), delving into biochemical facets associated with pathological conditions, and implementing extensive molecular modifications.[1,2]

A combinatorial synthesis strategy was enabled, which enabled rapid acquisition of combinatorial libraries, in order to reduce the required time to synthesize and purify large amount of lead molecules, pharmaceutical companies developed the combinatorial synthesis strategy which led to the development of High Throughput Screening methods (HTS) methods, where the compounds could be evaluated quickly.[3] Due to pharmacokinetic problems and toxicity, most of the compounds were reapproved during clinical trials.[5] Using combinatorial techniques it was possible to synthesize thousands of compounds.[4] Cancer is uncontrolled growth and division of abnormal cells at a faster rate than normal, which grow as a lump also called as tumour. In other words, it is abnormal, uncontrolled, progressive growth of cells. The growth of cell becomes uncontrolled when the programming of the cells is affected. It is noncontagious disease. Factors such as tobacco, smoke, dust, radioactive substances, age, sex, race and heredity can alter the code of chronic irritation.as we cannot control all the factors its essential to be aware of the ones we can control. Prevention is always better then cure.

The types of cancer[3-6]

Carcinoma: Cancer which affects organs and glands including lungs, breasts, pancreas and skin.it is most common type of cancer.

Sarcoma: It affects the connective tissues, such as muscle fat, bone, cartilage or blood vessels.

Melanoma: Cancer can be developed in the cells that pigment in the cells.

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Lymphoma: Cancer which affects lymphocytes or white blood cells.

Leukemia: Cancer which affects blood.

To thwart or curb the progression of carcinogenesis, the anticancer activity is attributed to the impact of both natural and synthetic agents, encompassing biological and chemical elements. Globally, breast cancer stands out as a predominant form of malignancy. There remains a pressing need for innovative therapies to enhance the survival rates of cancer patients, particularly those with estragon receptor/progesterone receptor/Human Epidermal growth factor (HER)2 negative conditions. Exploring potential cancer-fighting agents involves the identification and optimization of compounds found in various plants and animal species. A notable example is the manifestation of Antitumour activity in numerous marine alkaloids, leading to the discovery of new lead molecules sourced from sponges. The quest for novel cancer therapeutic agents has also given rise to the development of synthetic analogues, such as makaluvamine, derived from marine compounds. These synthesized compounds exhibit high potency against a spectrum of cancers, including breast cancer.[7-10]

Schiff base compounds are adaptable compounds which possess broad spectrum of biological activity by incorporation of metals in form of metal complexes. These compounds showed antibacterial, antitumor, anti-inflammatory activity. Compounds are modified for their pharmacological and toxicological properties in the form of metal complexes.[1] Schiff's base compounds were first reported by Hugo Schiff in 1864, where the Schiff's base compounds are the condensation products of ketones and aldehydes with primary amines. These compounds contain azomethine group (-HC=N-). The synthesis of Schiff's base compounds takes place under acid/base catalysis or with heat. The Schiff base compounds are generally crystalline solids, freely soluble in bases, some form insoluble salts with strong acids, which can be used for synthesis of metal complexes for ligand preparations As Schiff Base compounds have the capability of forming stable complexes with metal ions, showing excellent catalytic activity in various reactions, they have significant importance in chemistry. There have been various reports in the recent years regarding the application of Schiff's metal complexes in homogeneous catalysis which focuses on the catalytic activity.[11-15]

The Azomethane nitrogen and other donor atoms like oxygen play a significant role in forming the complexation. The Schiff base acts as a Flexi-dentate ligand and coordinates from the O atom of phenolic group and the N of azomethane group. Therefore, it is essential to study the interaction of the Schiff's base with the transition metal having pharmacological interest in coordination chemistry. We have described the synthesis and characterization of Schiff's base and their metal complexes in our present work.[16-20] It is observed that aliphatic aldehydes are unstable and readily polymerise whereas the aromatic aldehydes especially with effective conjugation form stable complexes. Schiff's base ligands are formed more easily with aldehydes then with ketones. As Schiff's bases are versatile, flexible and diverse in nature, a wide range of compounds and their behaviour is studied. They are most commonly di, tri, tetra-dentate ligands. These form stable complexes with metal ions. The physicochemical properties of Schiff's base were studied such as identification, determination of aldehydes and ketones, purification of carbonyl and amino compounds or synthesis of complexes.[21-30]

Molecular Docking is a computational molecular modification technique, which helps in the prediction of preferred binding site of ligand to receptor, when they form a stable complex by interaction.[31-39] Energy profiling such as binding free energy, strength and stability like binding affinity and binding constant of complexes and orientation of bound molecules, such information can be obtained using scoring function and molecular docking. It is recently used to forecast the binding orientation of small molecules to their bio-molecular target such as protein, carbohydrates and nucleic acids which helps to determine the tentative binding parameters which helps in rational drug designing (structure and ligand based drug design) and modelling with more specificity and efficacy. An optimised docked conformer of both interacting molecules is the major objective of molecular docking.[40-45]

Schiff's base metal complexes play a significant role in development of coordination chemistry. The DNA binding studies and cleavage properties under physiological conditions have attracted the curiosity to study transition metal complexes. There have been various reports in the recent years regarding the application of Schiff's metal complexes in homogeneous catalysis which focuses on the catalytic activity.[46-51]

MATERIALS AND METHODS

Materials

Chemicals

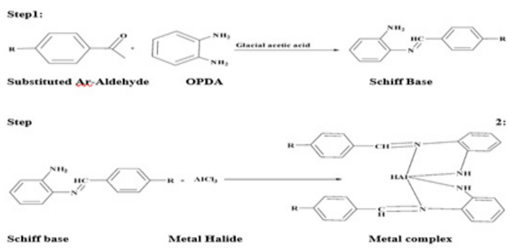
Chemicals used in this synthesis are Orthophenylene diamine and selected derivatives of benzaldehyde (Salicylaldehyde, 4-chlorobenzaldehyde, 4-Bromobenzaldehyde, Tolaldehyde and Anisaldehyde), Glacial acetic acid, methanol, ethanol (97%), chloroform, ethyl acetate, Conc. HCl.

Apparatus

RBF (Round bottom flask), Measuring cylinder, beakers, glass rod, reflux condenser, TLC plates, watch glass, heating mantle, iodine chamber, Theil's tube, magnetic stirrer with magnetic beads, capillary tubes, treads were used.

Methods

Methodology: General scheme of Synthesis of Schiff's base-metal complexes

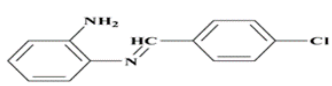


Synthesis of the Schiff bases generally carried out by reacting equimolar concentrations of substituted Aromatic aldehyde and Orthophenylene diamine (OPDA) in 20 mL ethanol/methanol. This reaction is based on simple condensation reaction. This mixture was refluxed with heating or by using a magnetic stirrer for about 6-8 hr. The product was obtained by filtration and it was recrystallized from ethanol and water. The prepared Schiff base compounds were subjected to complex with selected metal such as AlCl.[31-35]

RESULTS

Details of Schiff bases and corresponding metal complexes

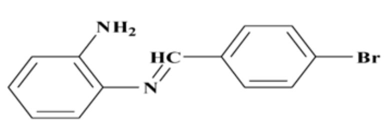
Schiff's base (E)-2-((4-chlorobenzylidine) amino) aniline



(*E*)-2-((4-chlorobenzylidene)amino)aniline

It was obtained as brown solid, yield: 67.3%, MP: 197°C. FTIR (KBr, cm^{-1}), 3508.67(N-H), 1600.02(C=C)1640(NH).

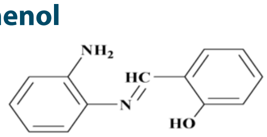
Schiff's base (E) -2-(4-bromobenzylidene) amino) aniline



(*E*)-2-((4-bromobenzylidene)amino)aniline

It was obtained as Cream coloured solid, yield: 71.2%, MP: 185°C. FTIR (KBr, cm^{-1}), 3415.12(NH), 1600.02 (C=C) and small peaks of Aromatic C-N and Br.

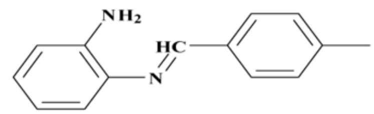
Schiff's base (E) -2-(((2-aminophenyl) imino) methyl) phenol



(*E*)-2-(((2-aminophenyl)imino)methyl)phenol

It was obtained as white solid, yield: 84.2%, MP: 191°C. FTIR (KBr, cm^{-1}), 3462(NH_2), 3513.49(OH), 1454.39(C=C).

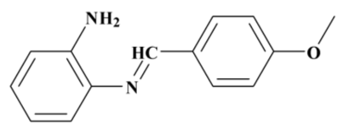
Schiff's base (E) -2((4-methylbenzlidene) amino) aniline



(*E*)-2-((4-methylbenzylidene)amino)aniline

It was obtained as white solid, yield: 83.1%, MP: 189°C. FTIR (KBr, cm^{-1}), 3039(-CH), 1462.1(-C=C)1233.53(-CNH_2).

Schiff's base (E) -2-((4_methoxybenzylidene) amino) aniline

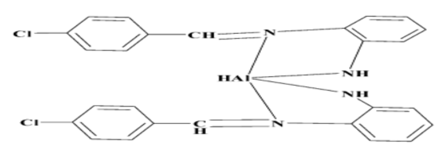


(*E*)-2-((4-methoxybenzylidene)amino)aniline

It was obtained as yellow solid, yield: 82.5%, MP: 178°C. FTIR (KBr, cm^{-1}), 1245.10(C=O) 3420(-NH).

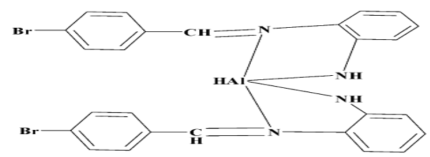
Metal complexes

MC-1



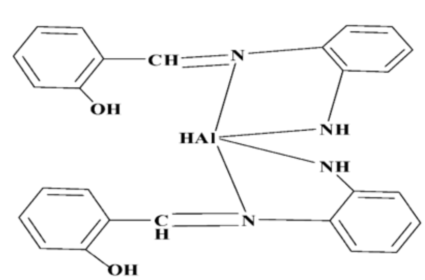
It was obtained as grey solid, yield: 85.2%, MP: 215°C. FTIR (KBr, cm^{-1}), 3413.16(NH)1584.89(C=N)1681.04(C=C)

MC-2



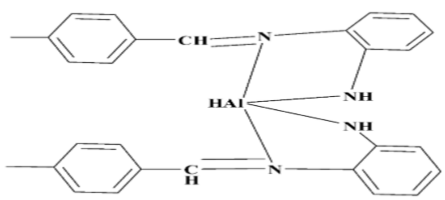
It was obtained as Cream solid, yield: 86.3%, MP: 247°C. FTIR (KBr, cm^{-1}), 1456.32(C=C) and also small peaks of (N=H) and (C=N).

MC-3



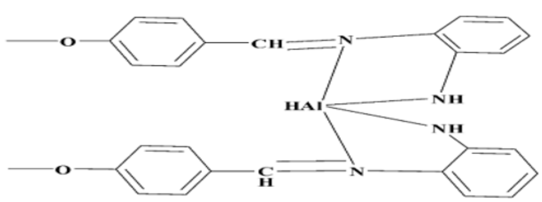
It was obtained as Cream solid, yield: 79.8%, MP: 212ºC. FTIR (KBr, cm^{-1}), 3551.10(N=H), 1456.32(C=C) and small peak of C=N.

MC-4



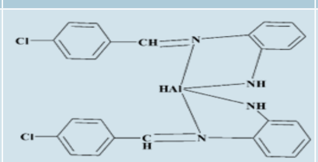
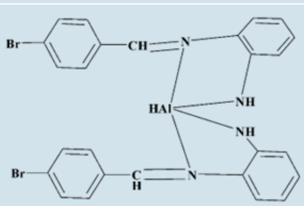
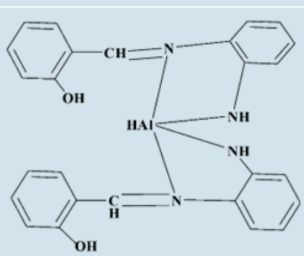
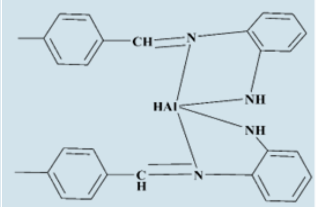
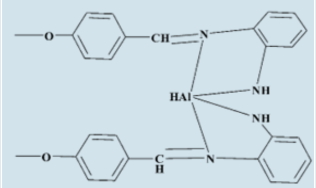
It was obtained as white solid, yield: 86.2%, MP: 249ºC. FTIR (KBr, cm^{-1}), 1600.029(C=C)3554(N=H)1646.32(NH), CH merged peak.

MC-5



It was obtained as white solid, yield: 89.5%, MP: 251ºC. FTIR (KBr, cm^{-1}), 1252.82(C-O)1643.42(N=H) 3431.51(NH) 3100(C-H).

Table 1: Details of the compounds.

Name of compound	Structure	Molecular weight	Physical appearance and yield
MC-1		452	
MC-2		496	
MC-3		433	White solid powder, 89.5%
MC-4		431	White solid powder, 86.2%
MC-5		447	White solid powder, 89.5%

Spectral Characterization

IR spectrum of Schiff's bases and Metal Complexes

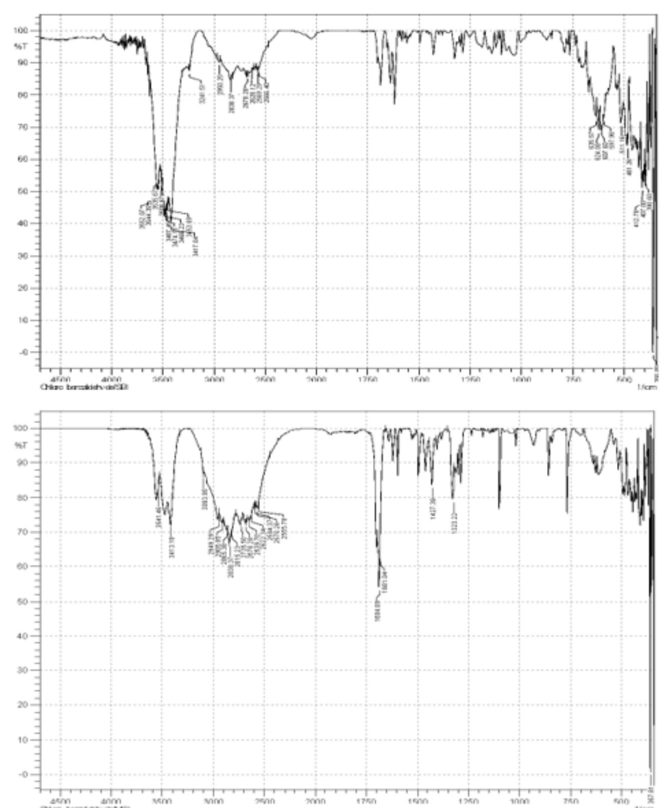


Figure 1: Infrared spectroscopy of SUS -1 and MC-1.

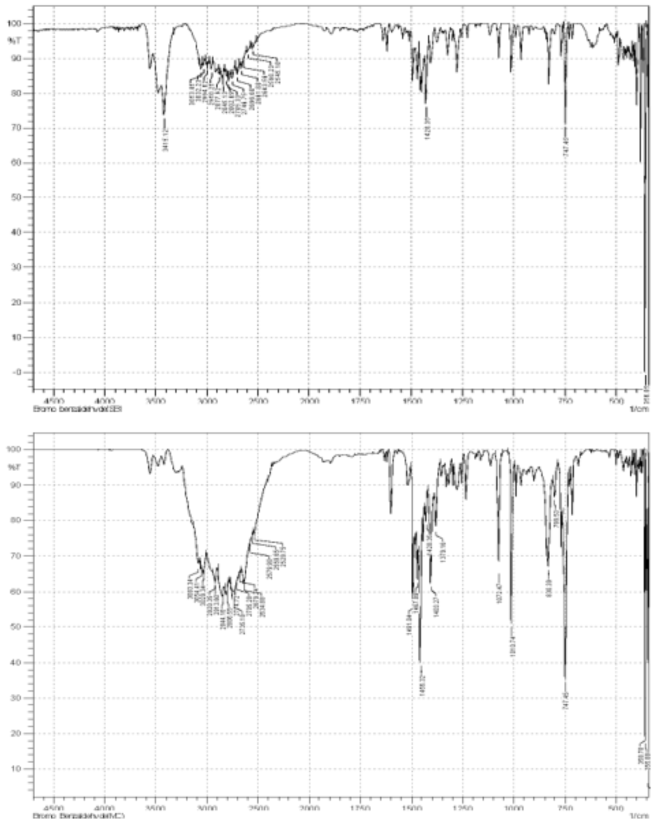


Figure 2 : Infrared spectroscopy of SUS -3 and MC-2.

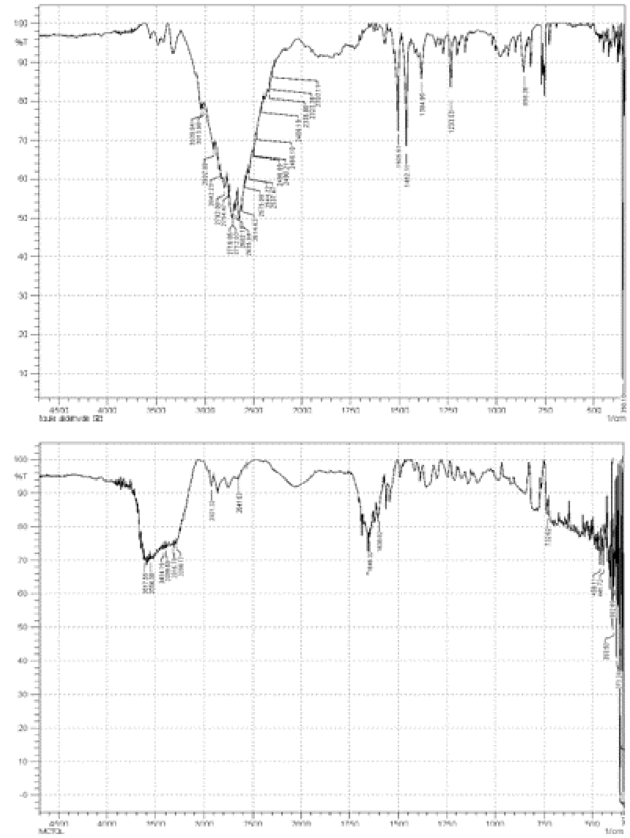


Figure 4: Infrared spectroscopy of SUS -7 and MC-4.

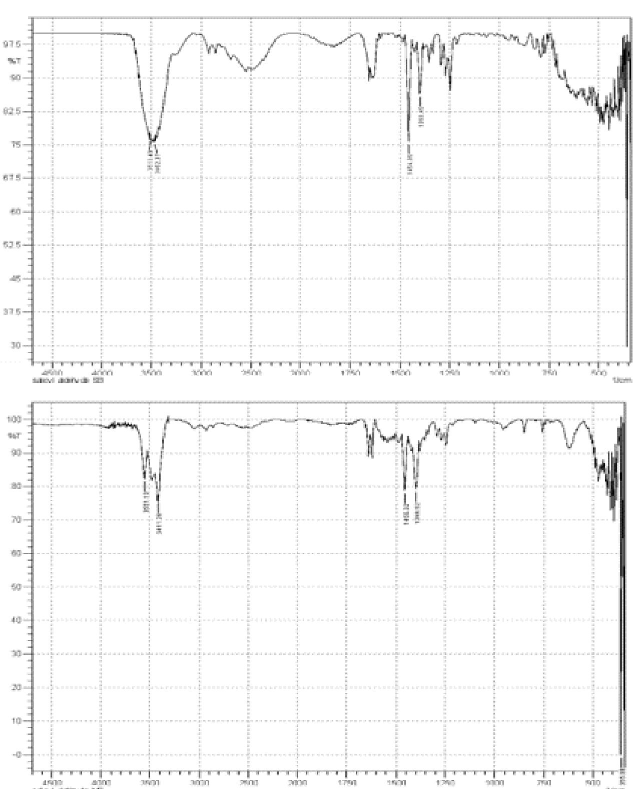


Figure 3: Infrared spectroscopy of SUS -5 and MC-3.

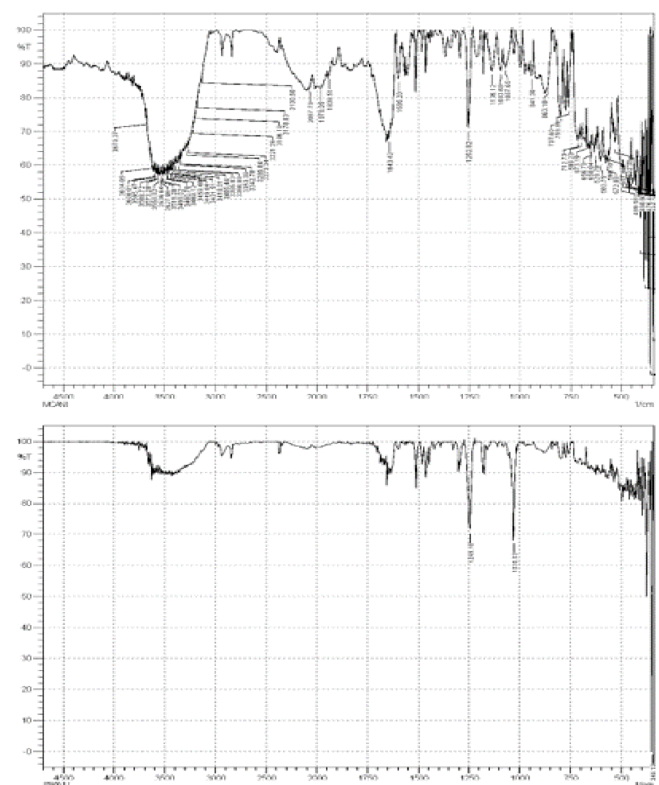


Figure 5: Infrared spectroscopy of SUS -9 and MC-5.

Table 2: FT-IR spectral data of Schiff's bases.

Name of compound	Characteristic vibration (cm^{-1})	Functional groups
2-((4-chlorobenzylidine) amino) aniline	3508.6 1600.02 1640	N-H, C=Cstr C-N
2-(4-bromobenzylidene) amino) aniline	3415.12 1600.02 Ar C-N.	NH, C=Cstr
2-(((2-aminophenyl) imino) methyl) phenol	3462 3513.49 1454.39	NH_2 Ph- OH C=Cstr
2((4-methylbenzlidene) amino) aniline	3039 1462.1 1233.53	C-H str C=C str C-NH_2
2-((4_ methoxybenzylidene) amino) aniline	1245. 3400 1660	-NH

Table 3: FT-IR Spectral data of organometallic complexes.

Name of Compound	Characteristic vibration (cm-1)	Functional groups
MC-1	3413.16 1584.89 1681.04	N-H str C=N C=C str
MC-2	1456.32 3200 1620	C=C N-H str C=N.
MC-3	3551.10 1456.32 1656	N-H str, C=C C=N.
MC-4	3039 1462.1 1233.53	-CH, -C=C C-NH_2
MC-5	1252.82 1643.42 3431.51 3100	C-O C=N N-Hstr C-H

NMR spectral data of metal complexes

Metal analysis (ICPMS) and SEM Report of Metal complexes

Anticancer activity (Cytotoxic activity) of Organometal Complexes by *In vitro* Cell line study.

TOL: Tolaldehyde (MC 1), **ANI:** Anisaldehyde (MC 2), **CBZ:** Chlorobenzaldehyde (MC-3), **SAL:** Salicylaldehyde (MC 4), Bromobenzaldehyde (MC 5).

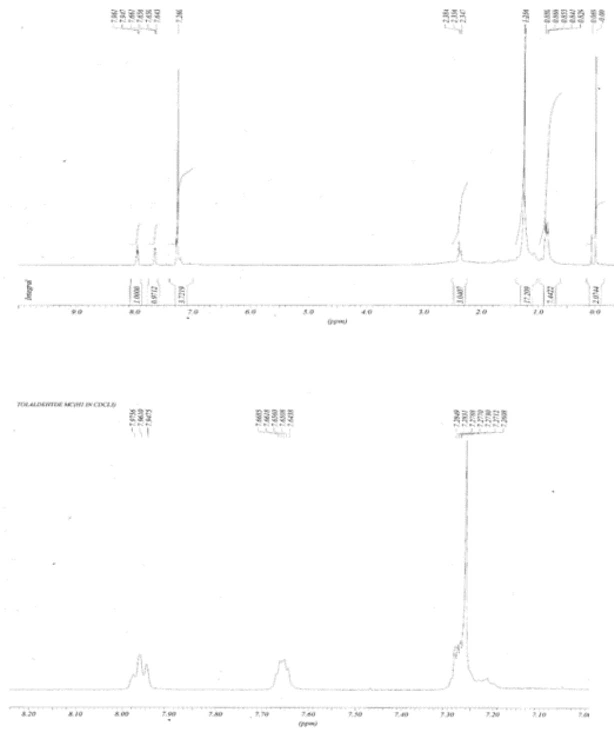


Figure 6: NMR spectrum of MC 1 (Tolaldehyde).

DISCUSSION

The Schiff bases which were synthesized by reacting substituted aromatic aldehydes with OPDA were subjected to preliminary identification by their melting points, T.L.C and IR study.

The I.R spectrum of Schiff bases (Figures: 1-5) were studied for characteristic vibrations of vital functional groups like NH_2, phenolic OH, CH=N, Ar-CH, C=C, -CHO mainly and these were identified in the spectrum of the Schiff bases. As the CH=N was mainly a significant group for the Schiff bases, it was found to be present in the spectrum and hence in the compounds.

Later, the synthesized Schiff bases were subjected to reaction with metal halide ($AlCl_3$) in EtOH/MeOH for 4-6 hr with magnetic stirring and in presence of glacial acetic acid (0.5 mL) which has improved the reaction and product formation. We have synthesized total five metal complexes of corresponding Schiff bases. These metal complexes were also subjected to preliminary identification by M.P, T.L.C and I.R data and recorded. The I.R (Figures 1-5) (Tables 2 and 3) and ^{1}H NMR (Figures 6-14) (Table 4) spectra of metal complexes was studied for the characteristic vibration mainly the chelation part and it was identified by its characteristic vibration in I.R spectra apart from all other vital groups like Phenolic OH, -NH_2 (OPDA), Ar-CH, C=C etc. These characteristic observations especially the metal chelate has confirmed although at the preliminary level the preparation of metal complexes.

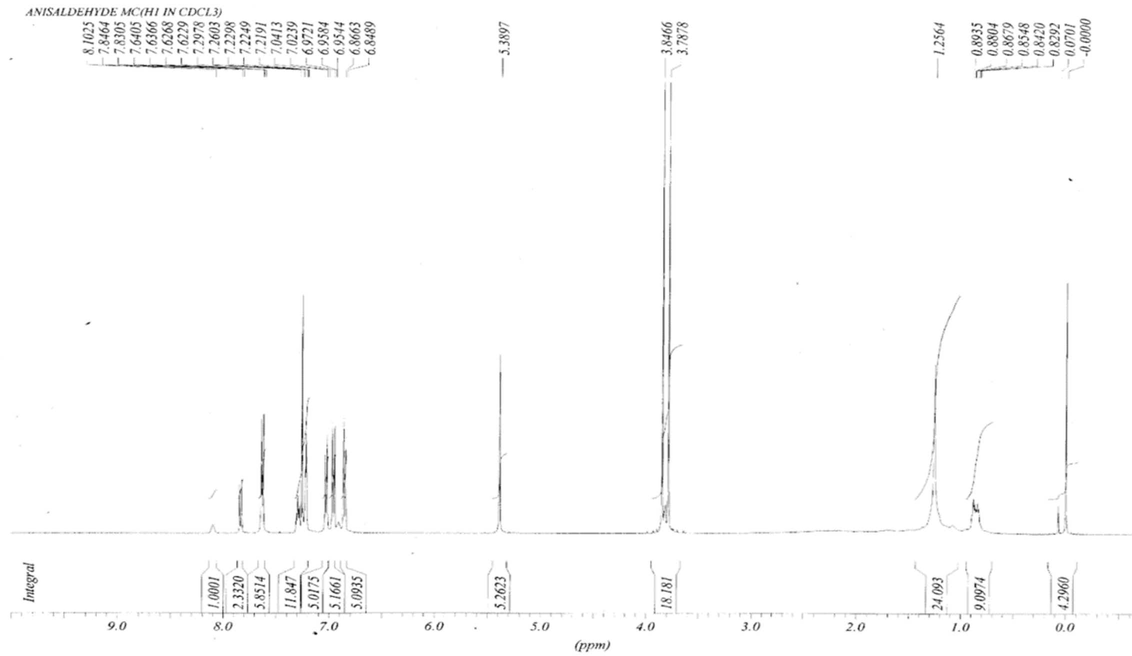


Figure 7: NMR Spectrum of MC 2 (Anisaldehyde).

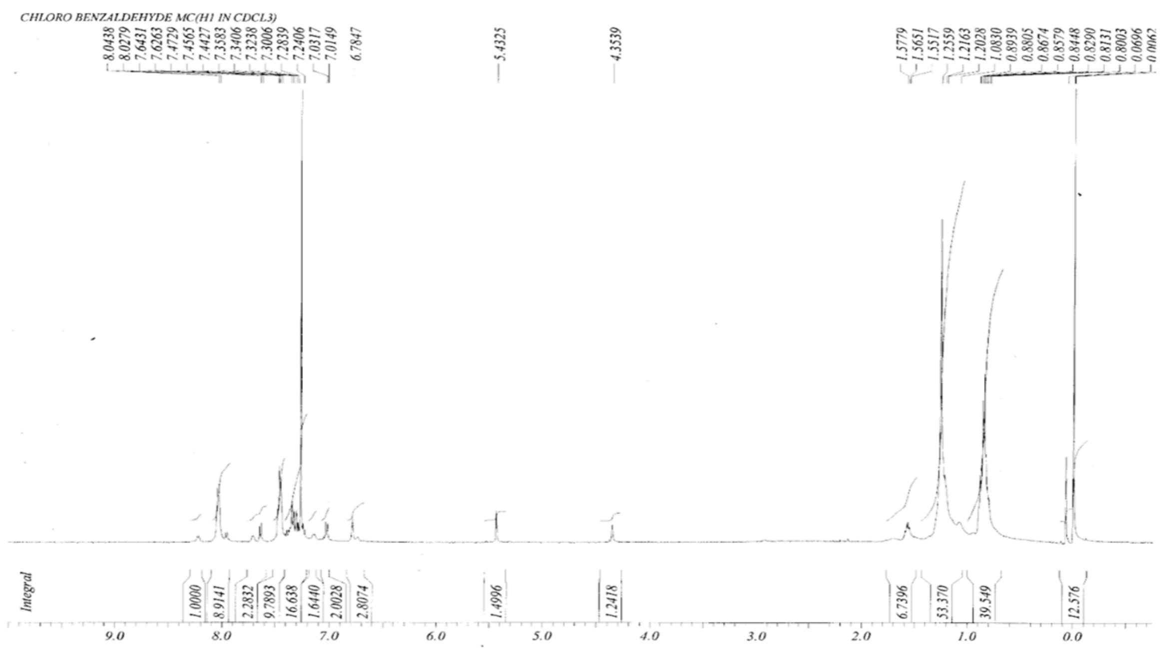


Figure 8: NMR Spectrum of MC 3(Chlorobenzaldehyde).

Docking is a method that predicts the preferred orientation and pose of ligand molecule within receptor, which in turn provides information regarding the interactions, binding affinity or strength of association between ligand and receptor by means of scoring functions. Docking algorithm fit molecules in complimentary fashions (Table 8).

The 3-dimensional protein structure of selected protein receptors present in *M. tuberculosis* and *M. smegmatis* were retrieved from Protein data bank (pdb). Docking study was performed using glide module of Schrodinger's molecular modelling software. (Schrodinger, Inc., USA, 2020-2), the docking of Schiff's bases (1-5) was carried out with the target protein and the study has

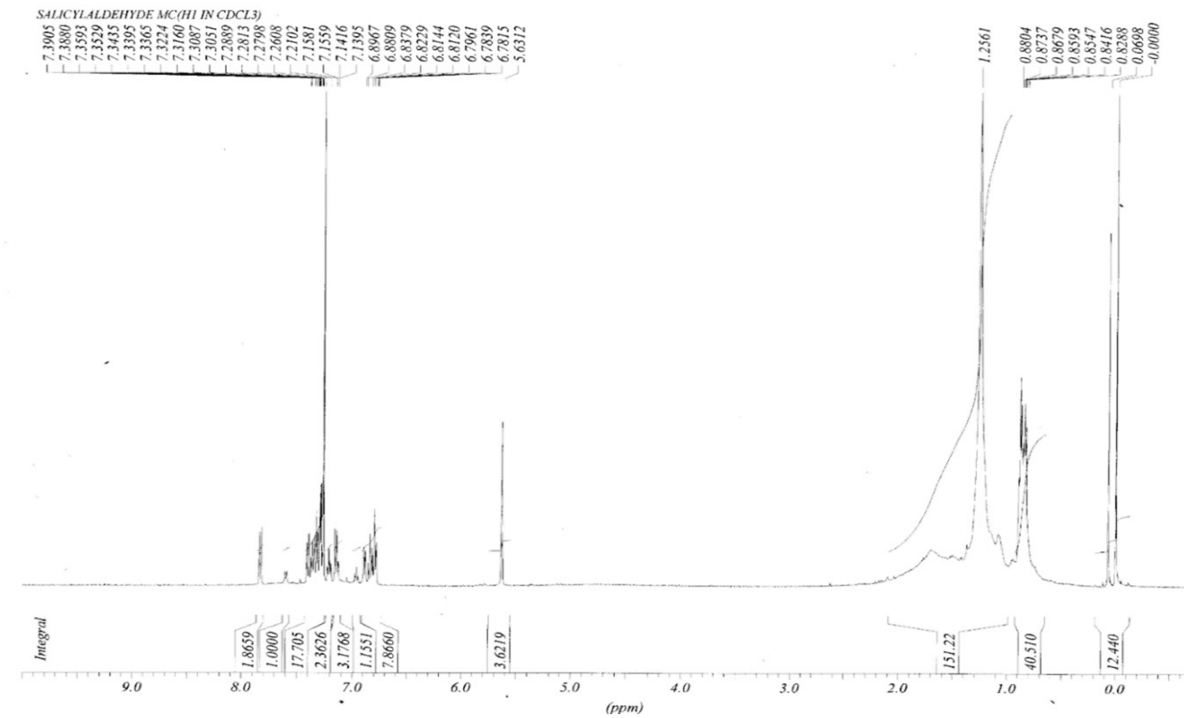


Figure 9: NMR Spectrum of MC 4 (Salicylaldehyde).

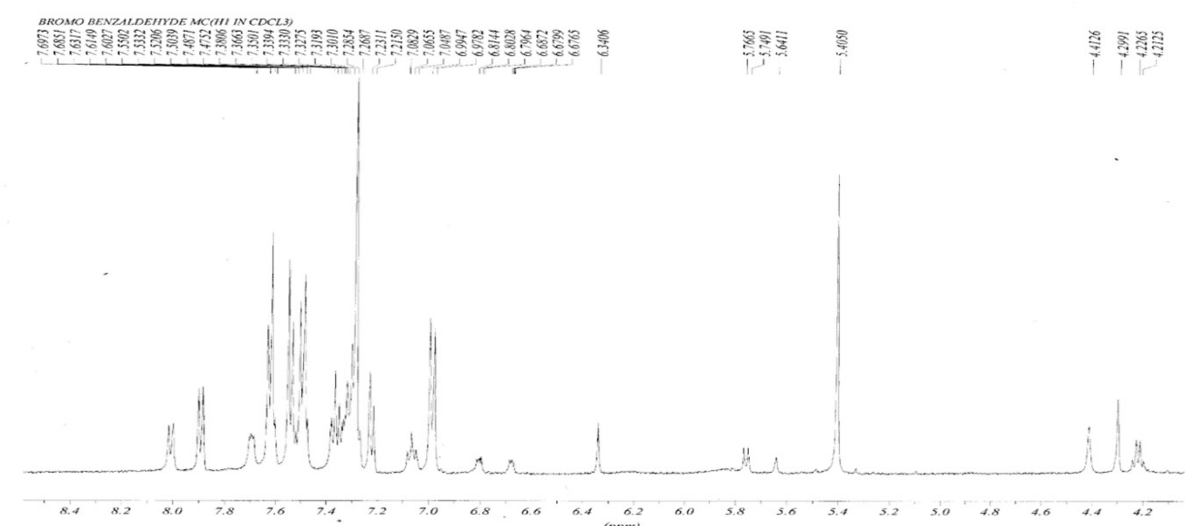


Figure 10: NMR Spectrum of MC 5 (Bromobenzaldehyde).

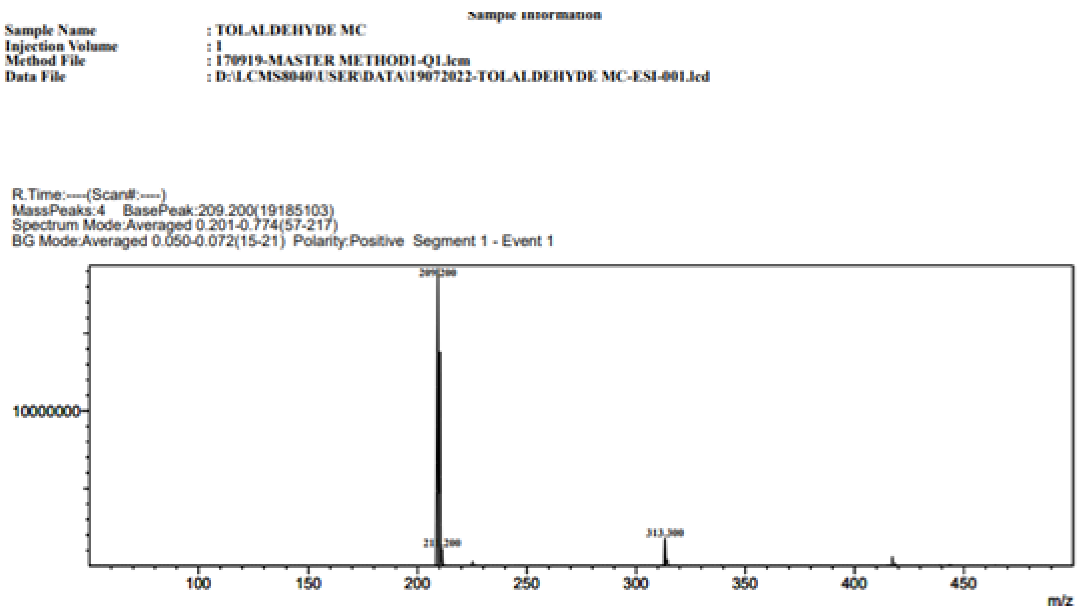


Figure 11: LCMS Spectrum of MC-1(Tolaldehyde).

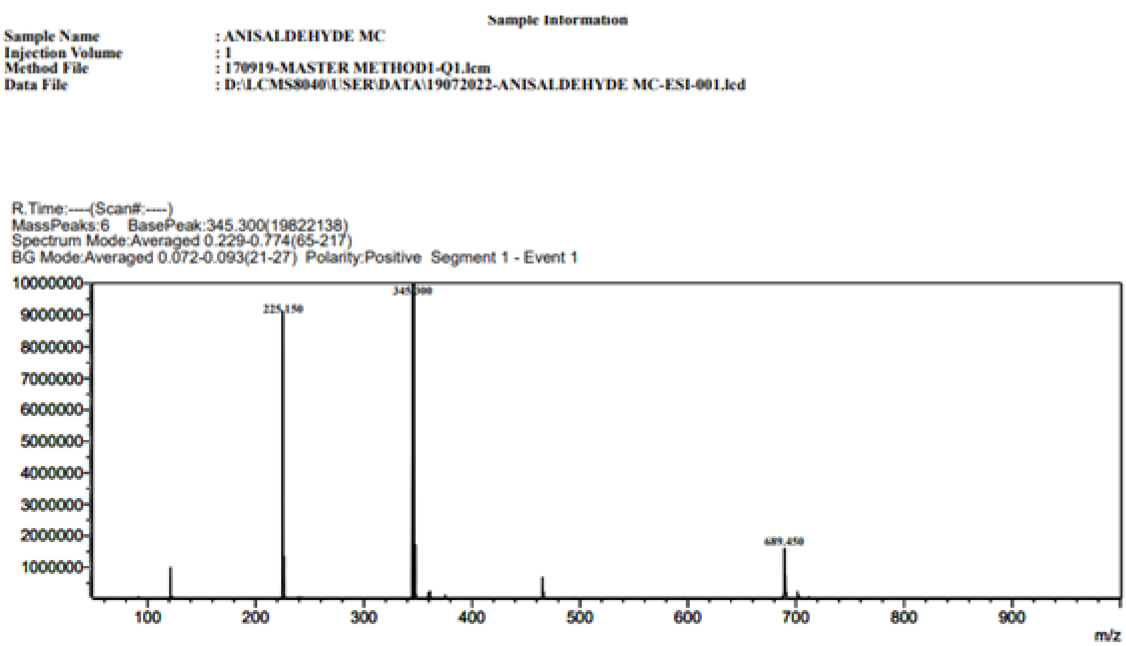


Figure 12: LCMS Spectrum of MC 2(Anisaldehyde).

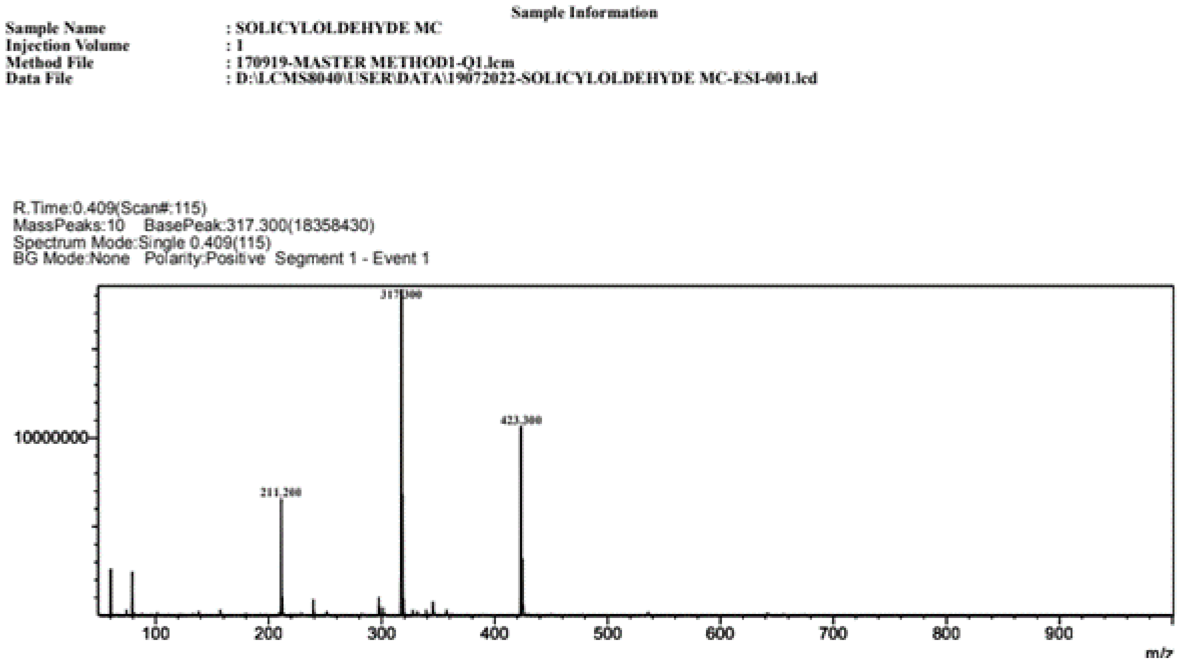


Figure 13: LCMS Spectrum of MC-4 (Salicylaldehyde).

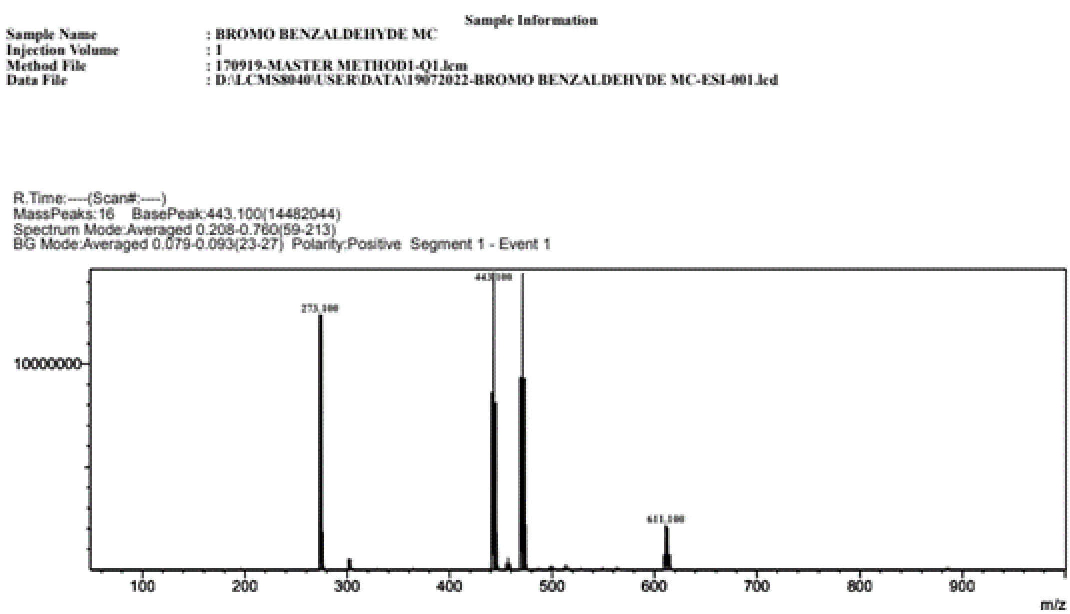
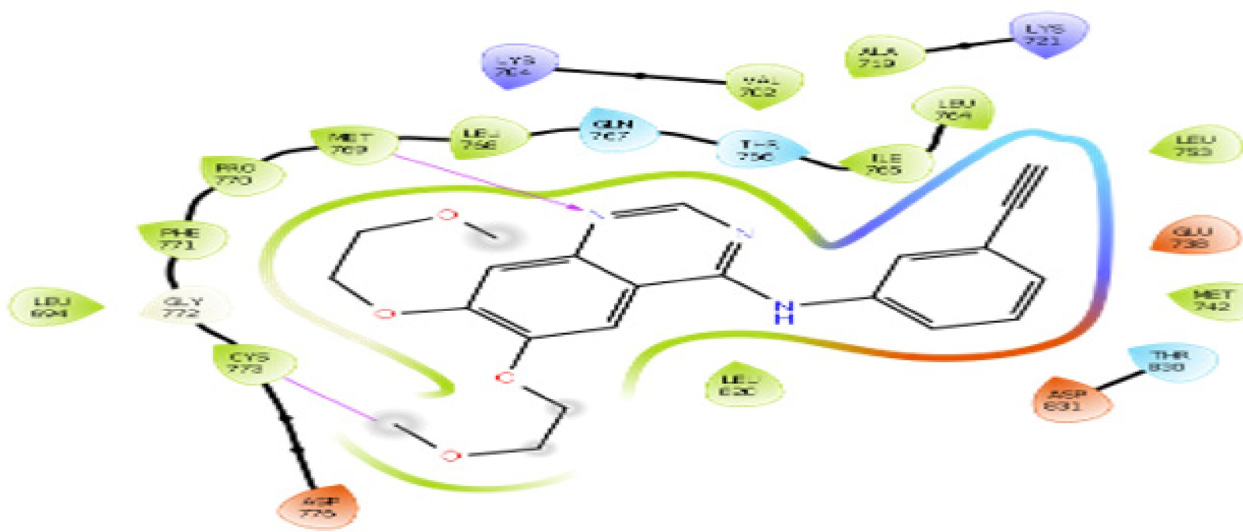


Figure 14: LC MS Spectrum of MC-5 (Bromobenzaldehyde).



ERLOTINIB

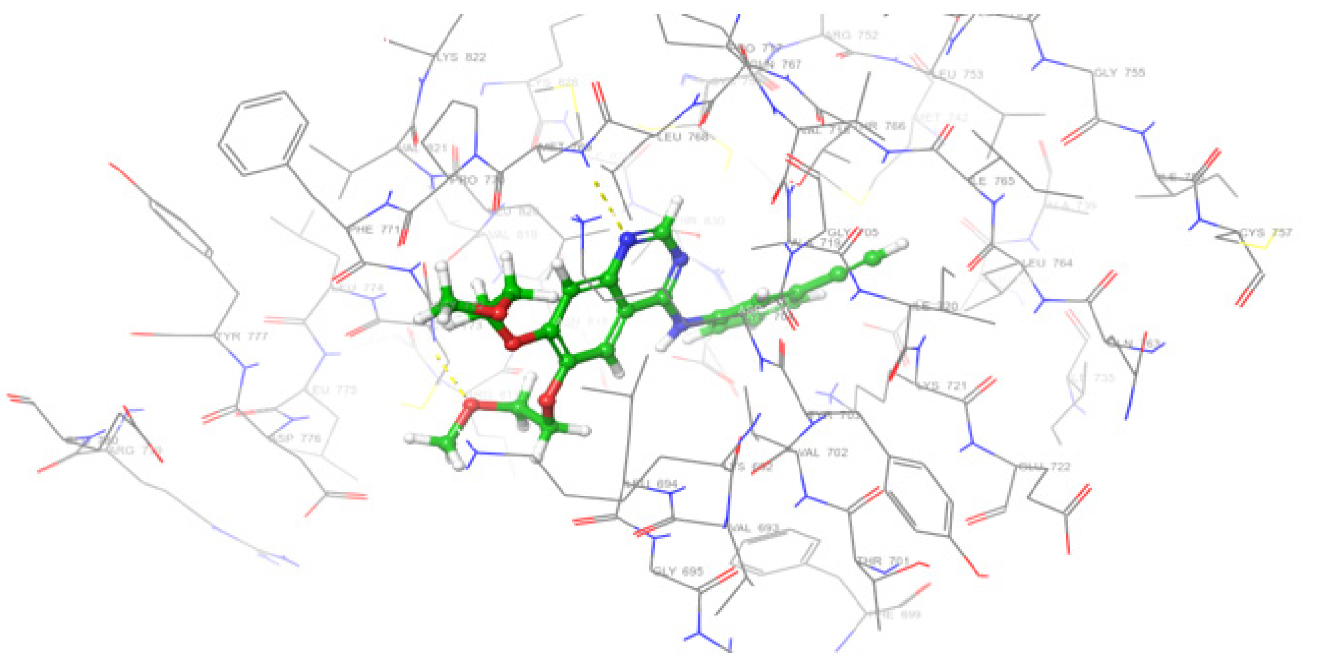
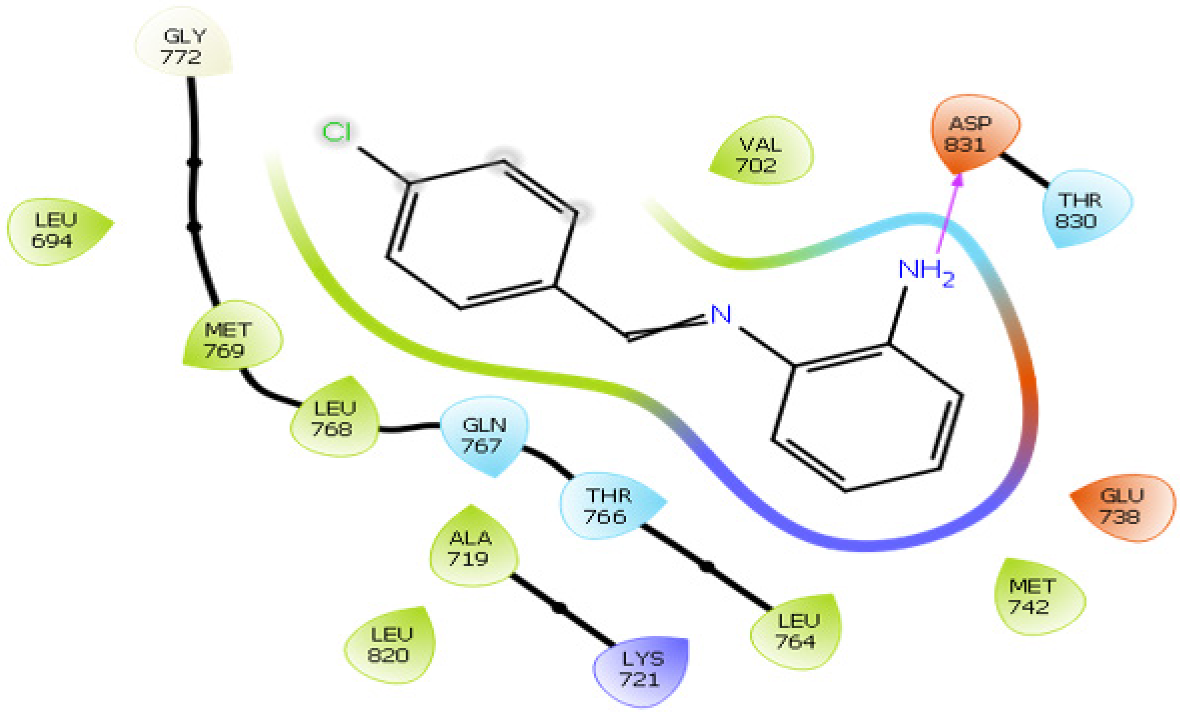


Figure 15: Pose of Erlotinib in tyrosine kinase (1M17) pocket: Pi- cation interaction with nitrogen atom of MET 769 and it also forms bond between carbon and CYS 773.

generated g-scores and the glide-energy required for docking with the target (Figures 15 to 26) and (Tables 5 to 7).

The LCMS spectrum of the metal complexes is studied and found that the molecular ion peak has indicated the formation of the metal complexes. This has justified the molecular weight of the complexes. The LCMS of MC-1 has shown the peak at 448 (m-2) which is approximately near its molecular weight (442). The LCMS of MC-2 has shown the peak at 465 and the molecular weight is found to be 496. The LCMS of MC-4 is 428(molecular weight is 431). The LCMS of MC-5 has shown a major peak at 420 and its molecular weight is found to be 447. Although the peaks do not match with m+ ion peak, however the observed peaks indicate the formation of metal complexes which might have



SUS-1

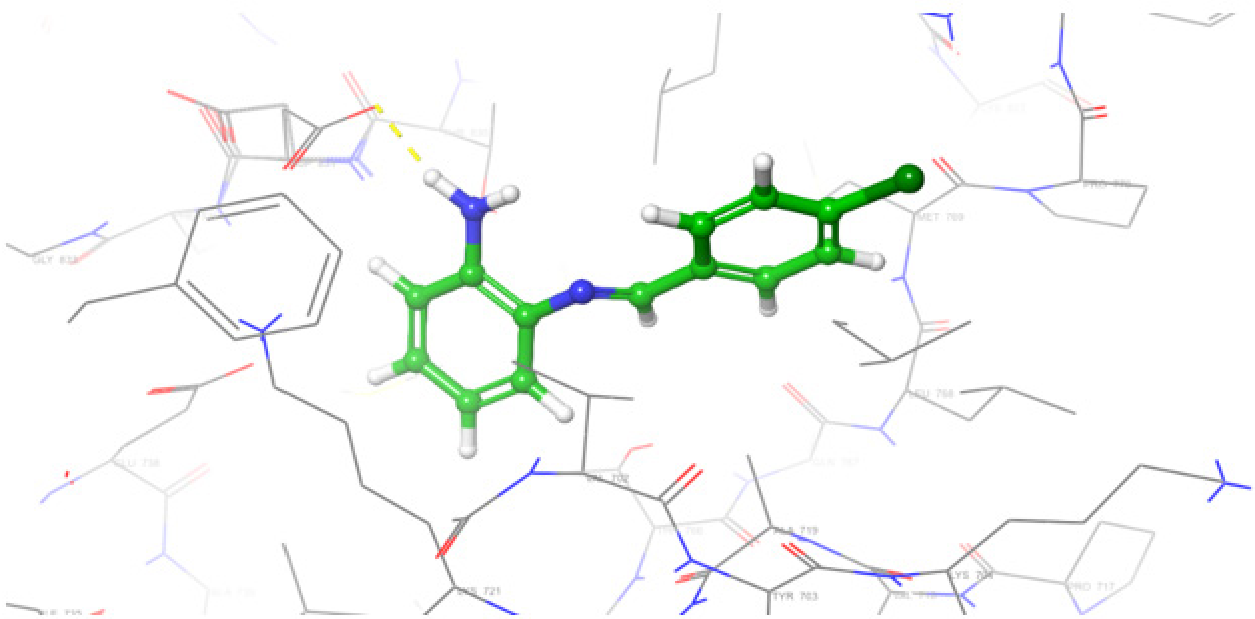
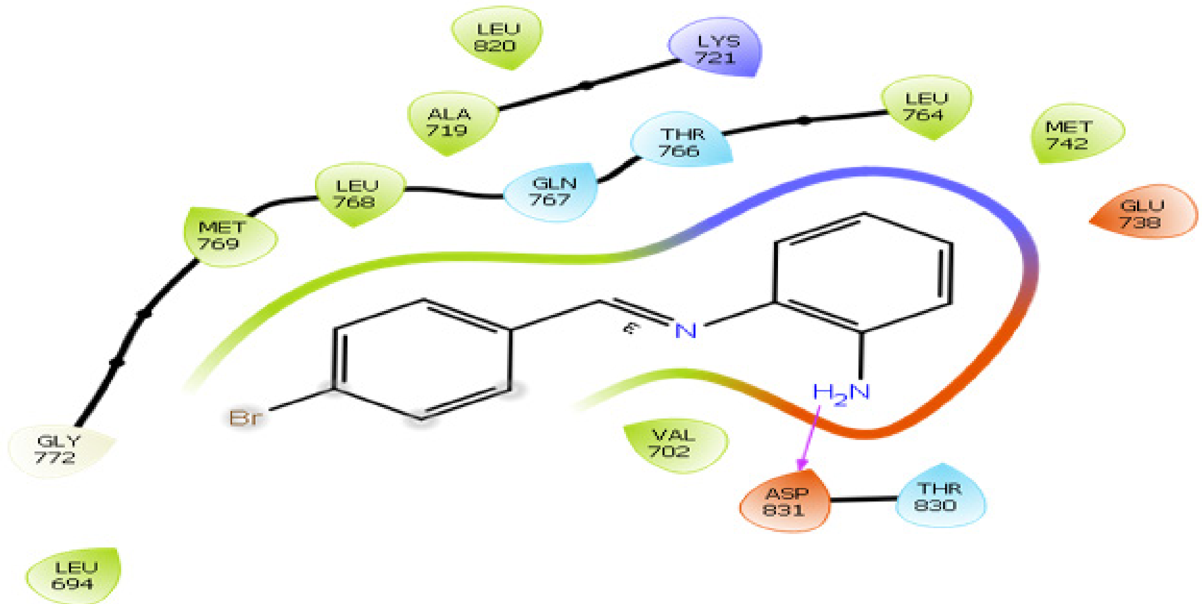


Figure 16: Pose of SUS-1 in tyrosine kinase (1M17) pocket: cation interaction of NH_2 with ASP831.



SUS-3

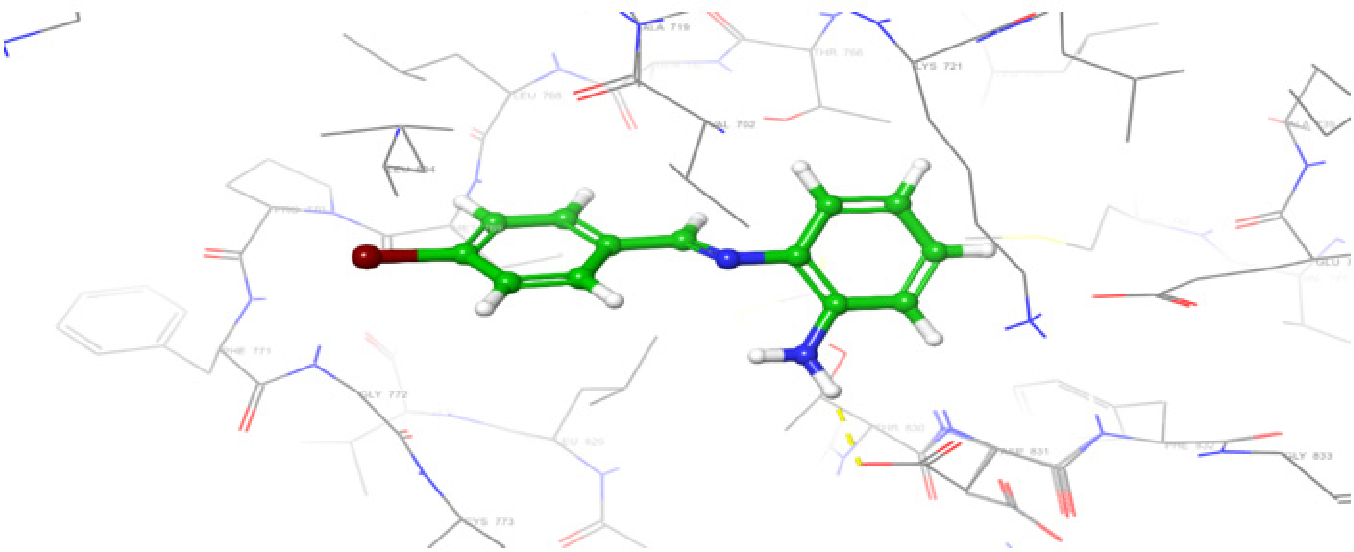
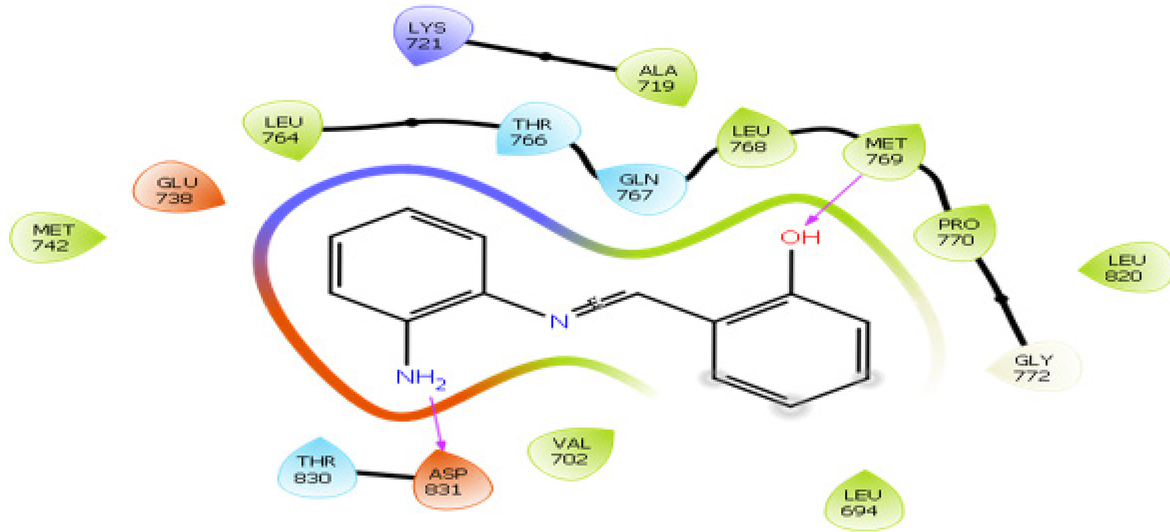


Figure 17: Pose of SUS-3 in tyrosine kinase (1M17) pocket: cation interaction of NH_2 with ASP831.



SUS-5

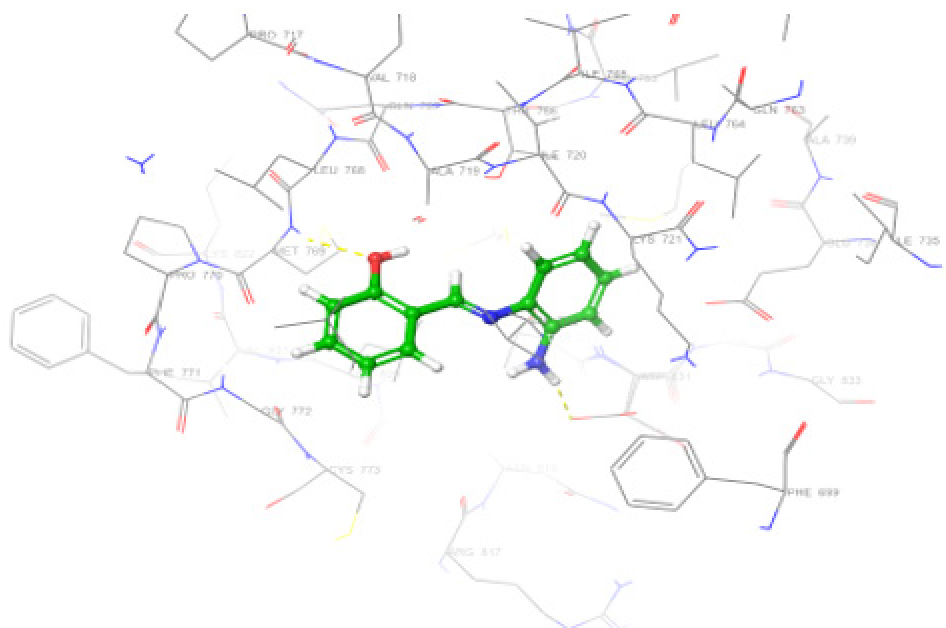


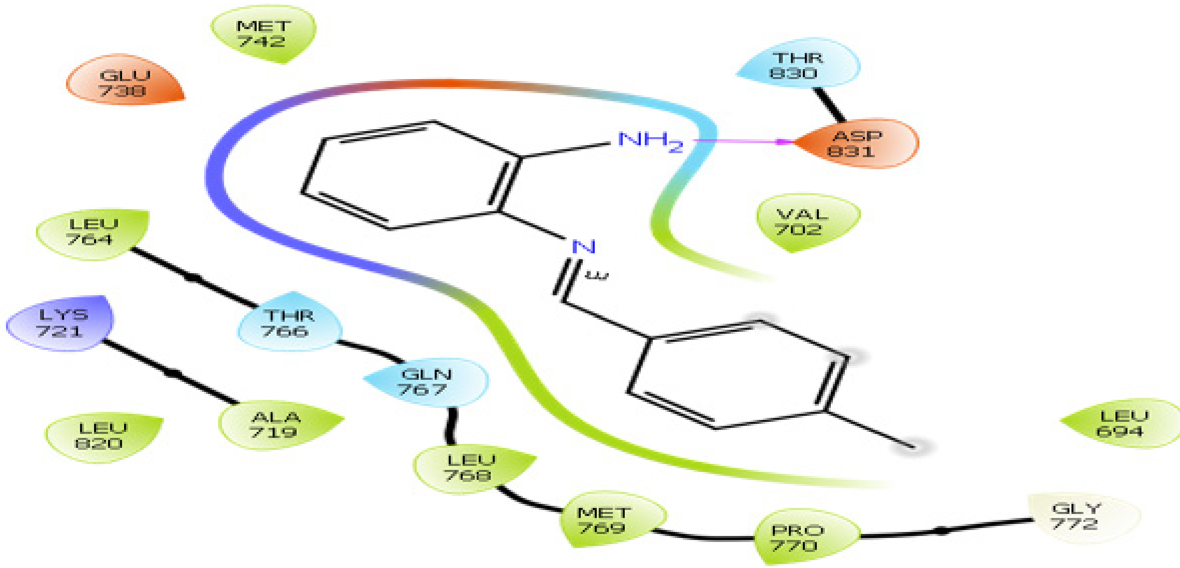
Figure 18: Pose of SUS-5 in tyrosine kinase (1M17) pocket: cation interaction of NH_2 with ASP831.

undergone fragmentation or some other chemical changes within the molecule. Hence, they differ with m+ ion with some units.

The SEM analysis and ICPMS study of the metal complexes were conducted and the reports highlighted the presence of the metal chelated with the organic material. As evident from the report, Aluminium metal is found to be present (report 1and 2)-5.14%. The report has shown the peaks for the Aluminium metal also. The ICPMS results indicate that chelation of Aluminium with the organic material (Schiff's base) is done successfully (Table 9).

The Scanning Electron Microscopy pictures of the organometal complexes shown the presence of metal embedded in organic material (Figures 30 and 31).

The cell toxicity study and cell viability study of organometal compounds (MC1-5) was conducted and the study results were analysed to know the cytotoxic effects of metal compounds on target cell line against standard drug Doxorubicin. The study results were promising and highlighted the cytotoxic potential of the metal compounds. The IC50 values of the organometal compounds (1-5) indicated that all the compounds are potential



SUS-7

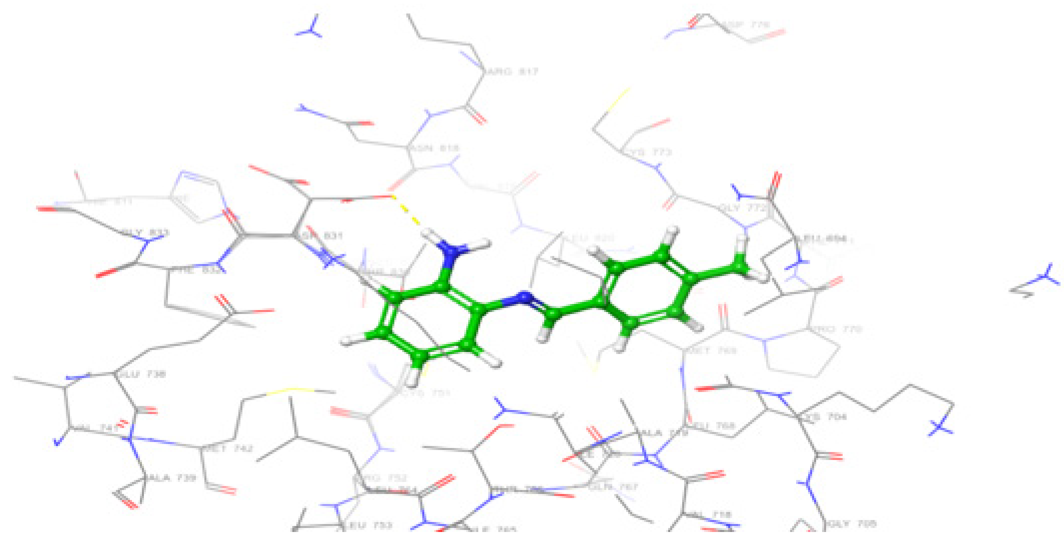


Figure 19: Pose of SUS-7 in tyrosine kinase (1M17) pocket: Pi- cation interaction NH_2 with ASP831.

enough to kill the cells; however MC-1(ANI) is 12.08 followed by MC-3(CBZ) at 15.96 which are close to the NIH limit of 10 and the highest being MC-5 (Tol)-128.03. The remaining are although less than highest (MC-5) but still more cytotoxic in nature than the standard (1.81). The viability study result shows that these metal complexes were successful in destroying the infected cells in comparison with standard.

The compounds were evaluated for their *in silico* docking studies using Schrodinger's glide software to study their antitumour potentials and all the compounds displayed good interaction with active pocket of tyrosine kinase (1M17) and EGFR kinase (2ITO). This indicates that their corresponding metal complexes could be potential anticancer agents. These organometal complexes were characterised by spectral data like IR, HNMR, LCMS and ICPMS. This spectral data has confirmed the compounds and ICPMS have indicated the presence of Al metal in the organic material. These organometal complexes were evaluated for their antitumour potentials by *in vitro* method against different strains of cell line cultures which has shown that most of the compounds are potential cytotoxic in nature and MC-1(ANI) and MC-3(CBZ) were safe as their IC50 values (12.08 and 15.96 respectively) were near the range of NIH (10). Hence, we anticipate that although all the synthesized organometal complexes are potential cytotoxic

Table 4: NMR spectral data of metal complexes.

Name of compound	Nature of proton (H vibration)	Spectral data (δ ppm)
MC-1	CH3, Aromatic protons, CH=N	1.9-1.8 7.9-7.6, 8.9-8.8
MC-2	CH3, Aromatic protons, CH=N	1.9-1.8 7.9-7.6, 8.9-8.8
MC-3	CH3, Aromatic protons, CH=N	1.9-1.8 7.9-7.6, 8.9-8.8
MC-4	CH3, Aromatic protons, CH=N	1.9-1.8 7.9-7.6, 8.9-8.8
MC-5	CH3, Aromatic protons, CH=N	1.9-1.8 7.9-7.6, 8.9-8.8

Table 5: LCMS Spectral data of metal complexes.

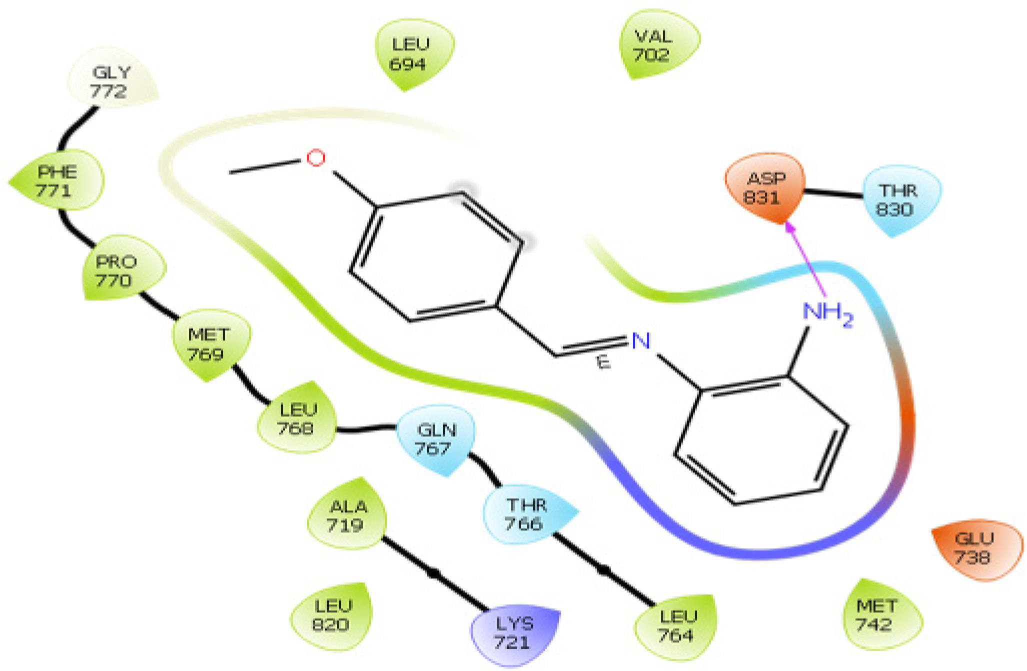
Name of compound	Mol^{r} weight
MC-1	452
MC-2	496
MC-3	433
MC-4	431
MC-5	447

Table 6: Molecular docking results of Schiff bases (ERLOTINIB).

Title	Docking score	Glide gscore	Glide emodel	glide energy
1M17-minimized				
ERLOTINIB	-8.296	-8.296	-79.52	-55.074
SUS-1	-6.629	-6.629	-49.467	-35.122
SUS-3	-6.556	-6.556	-50.587	-36.048
SUS-5	-6.989	-6.989	-53.292	-36.866
SUS-7	-6.696	-6.696	-48.785	-34.632
SUS-9	-6.823	-6.823	-50.986	-36.175

Table 7: Molecular docking results of Schiff Bases (GIFITINIB).

Title	Docking score	Glide gscore	Glide emodel	Glide energy
2ITO- minimized				
GIFITINIB	-7.412	-7.412	-71.978	-51.856
SUS-1(a)	-6.486	-6.486	-47.232	-33.529
SUS-3(a)	-6.29	-6.29	-47.783	-34.132
SUS-5(a)	-7.442	-7.442	-51.197	-34.759
SUS-7(a)	-6.435	-6.435	-46.051	-32.684
SUS-9(a)	-6.507	-6.507	-48.543	-34.488



SUS-9

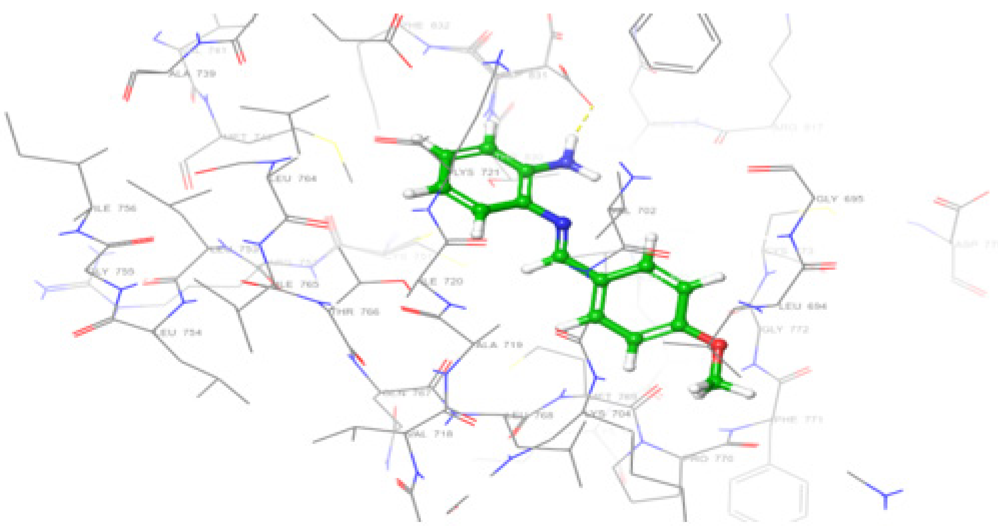
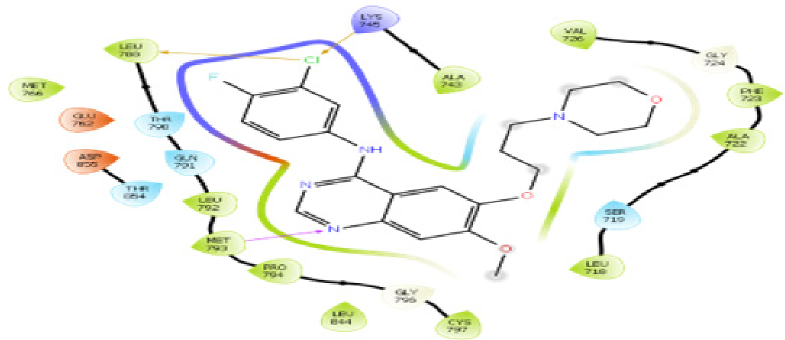


Figure 20: Pose of SUS-9 in tyrosine kinase (1M17) pocket: Pi- cation interaction of NH_2 atom with ASP831.

Table 8: Docking scores.

	Docking scores in Kcal/ mol	
Compound	1M17	2ITO
SUS-1	-6.629	-6.486
SUS-3	-6.556	-6.29
SUS-5	-6.989	-7.442
SUS-7	-6.696	-6.435
SUS-9	-6.823	-6.507



GIFITINIB

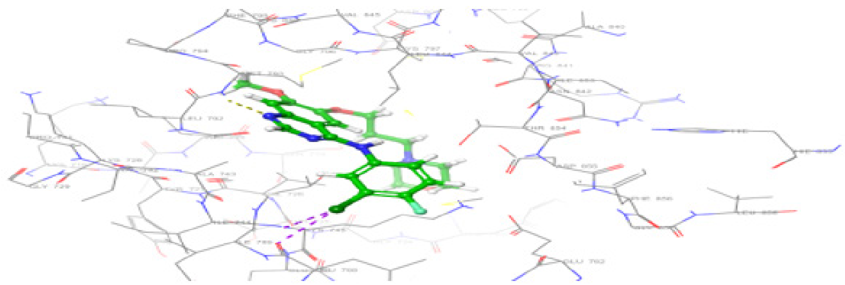
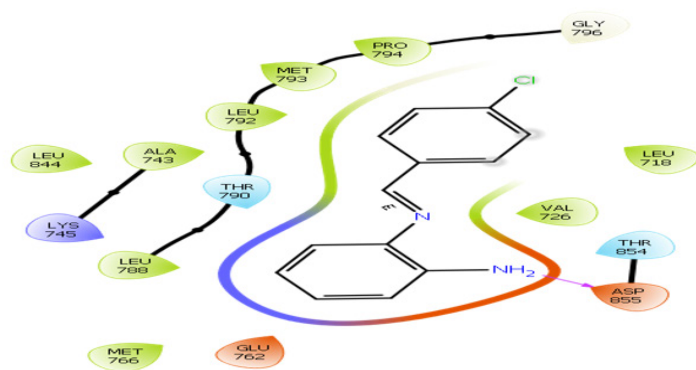


Figure 21: Pose of Gifitinib in EGFR kinase (2ITO) pocket: Pi- cation interaction with nitrogen atom of MET 793 and it also forms bond between chlorine with LYS-745 and LEU-788.



SUS-1(a)

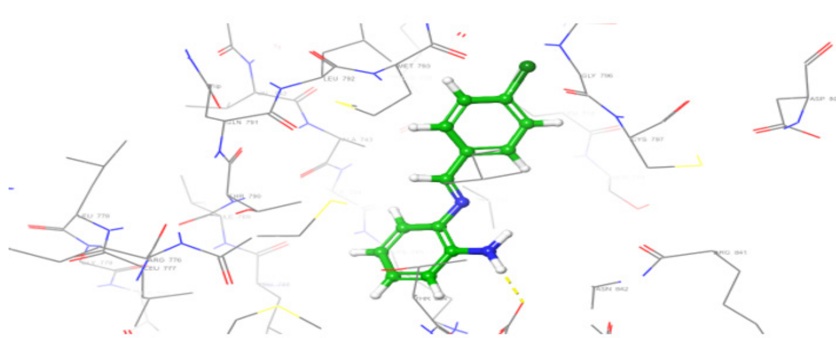
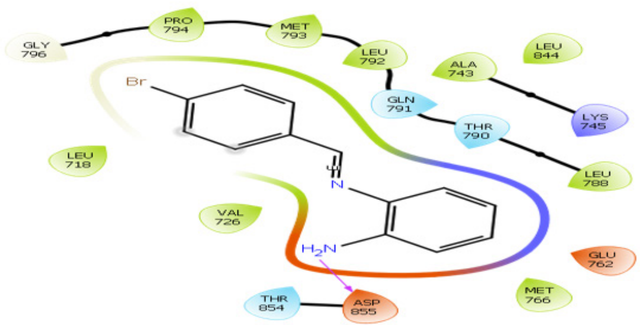


Figure 22: Pose of SUS-1 in EGFR kinase (2ITO) pocket: cation interaction of NH_2 with ASP-855.



SUS-3(a)

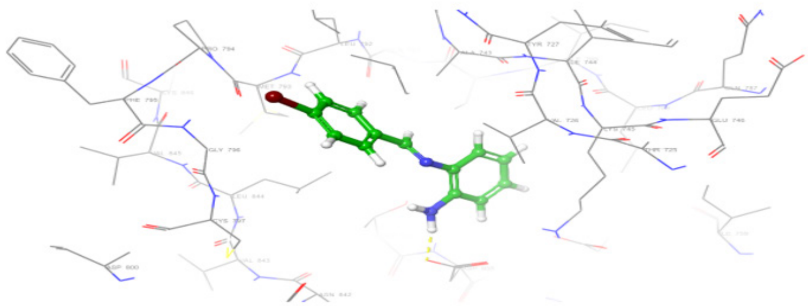
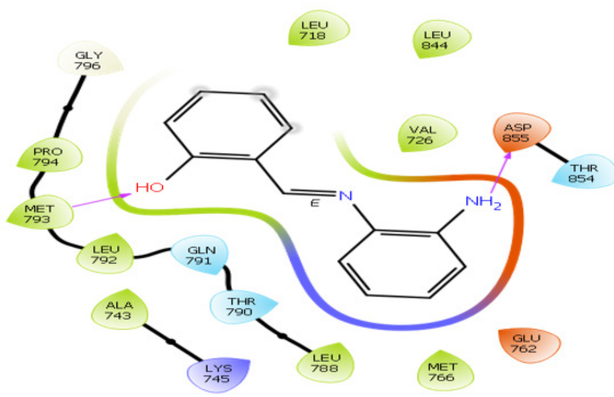


Figure 23: Pose of SUS-3 in EGFR kinase (2ITO) pocket: cation interaction of NH_2 with ASP-855.



SUS-5(a)

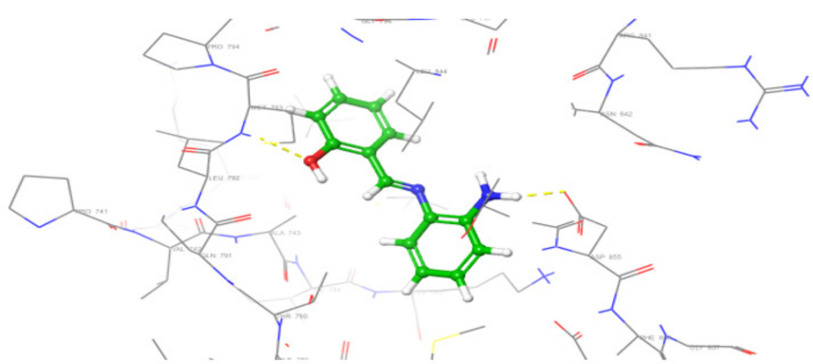
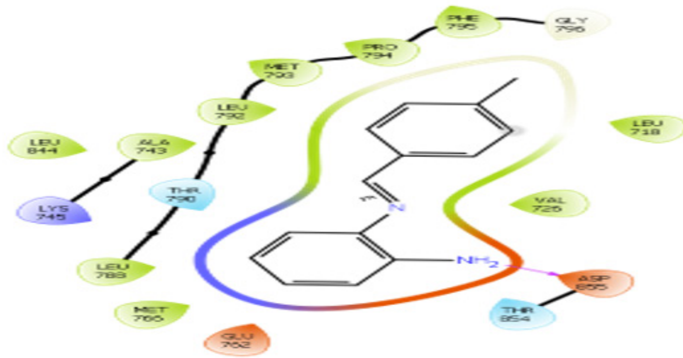


Figure 24: Pose of SUS-5 in EGFR kinase (2ITO) pocket: cation interaction of NH_2 with ASP-855 and also it forms bond between OH and MET-793.



SUS-7(a)

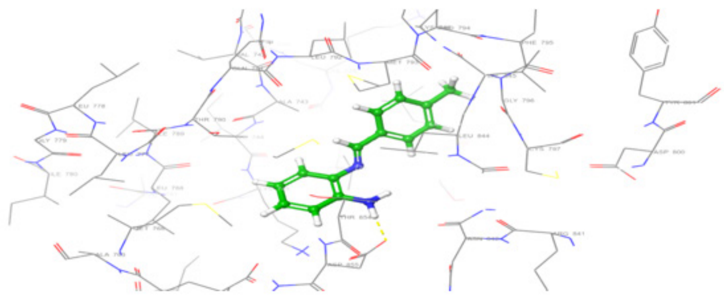
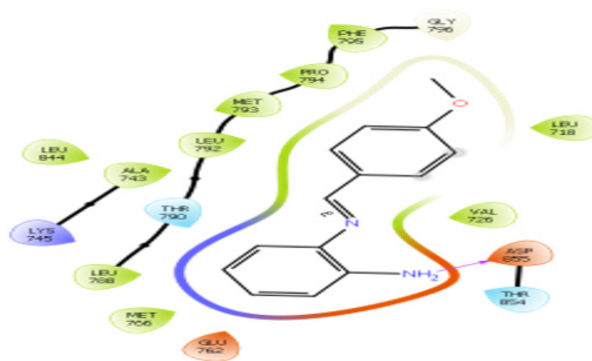


Figure 25: Pose of SUS-7 in EGFR kinase (2ITO) pocket: cation interaction of NH_2 with ASP-855.



SUS-9(a)

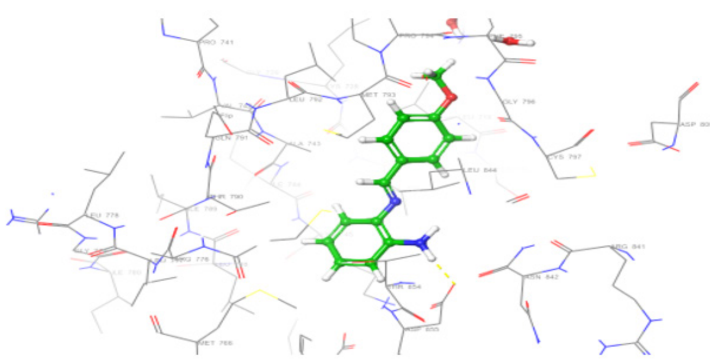
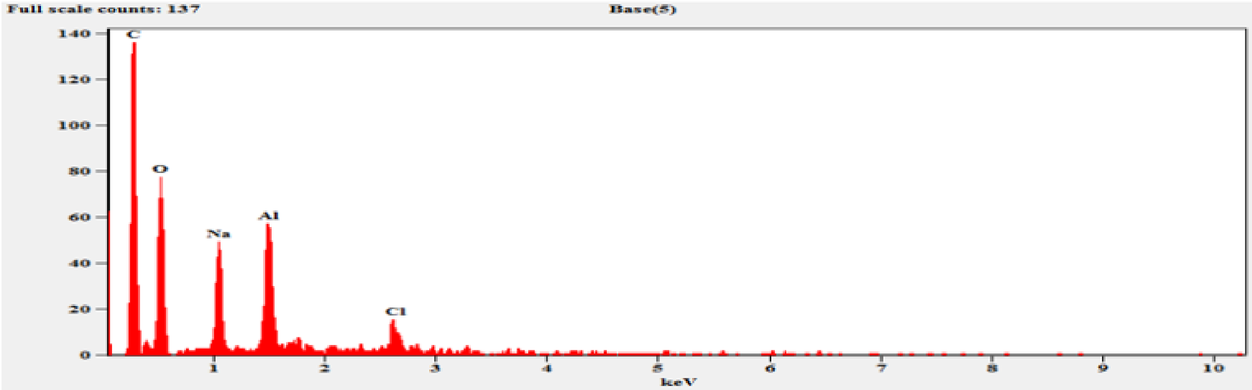


Figure 26: Pose of SUS-9 in EGFR kinase (2ITO) pocket: Cation interaction of NH_2 with ASP-855.



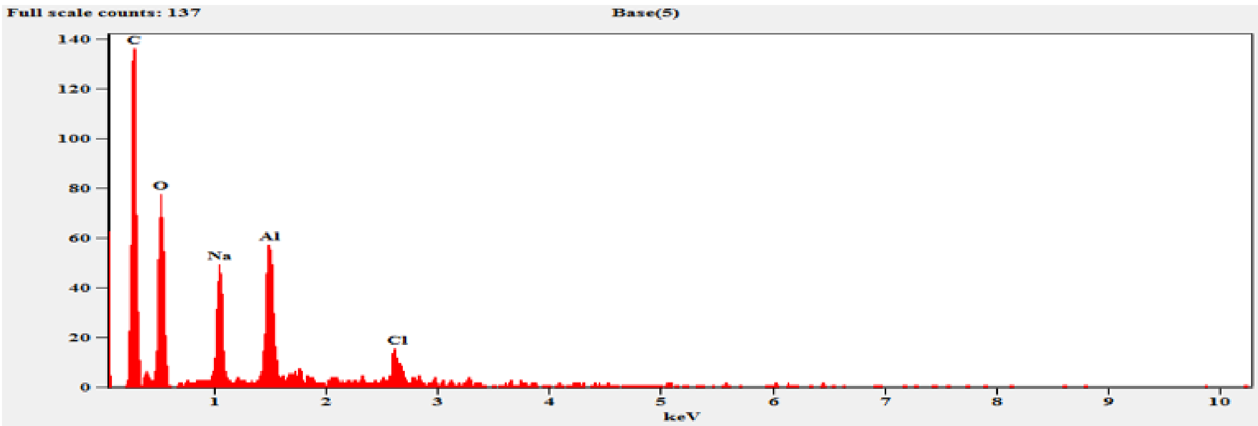


Table 9: Quantitative Results for Base (ICPMS).

Element Line	Weight %	Weight % Error	Atom %
C K	52.79	±4.61	62.52
O K	33.68	±2.41	29.95
Na K	6.70	±0.57	4.15
Al K	5.14	±0.33	2.71
Cl K	1.68	±0.19	0.67
Cl L	---	---	---
Total	100.00		100.00

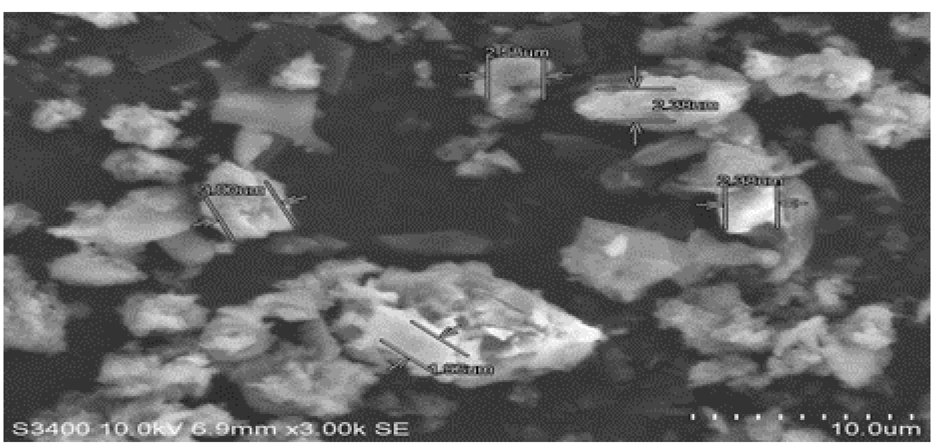


Figure 27: SEM picture of MC-1.

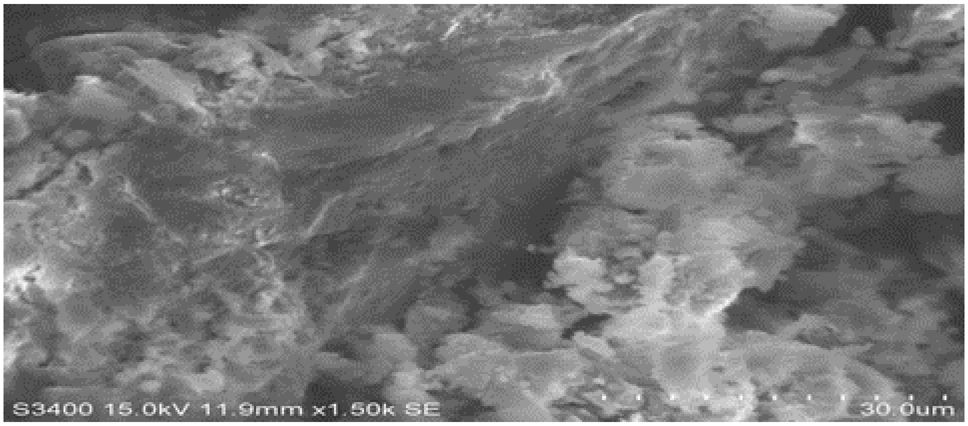


Figure 28: SEM Scanning picture of MC 2.

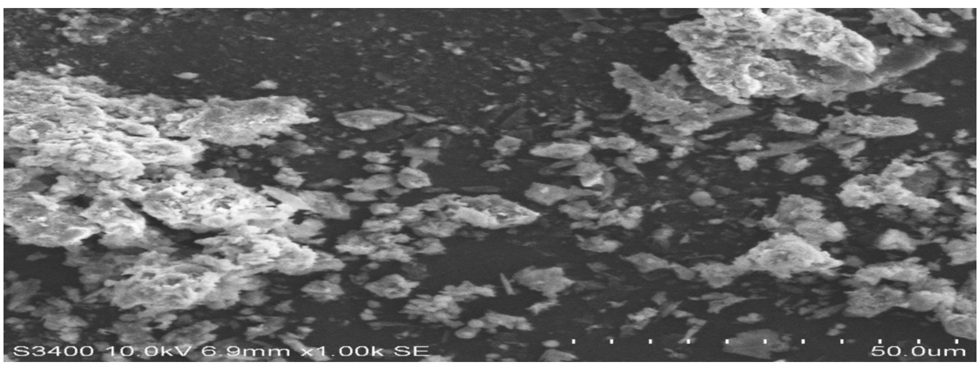


Figure 29: SEM Scanning picture of MC 3.

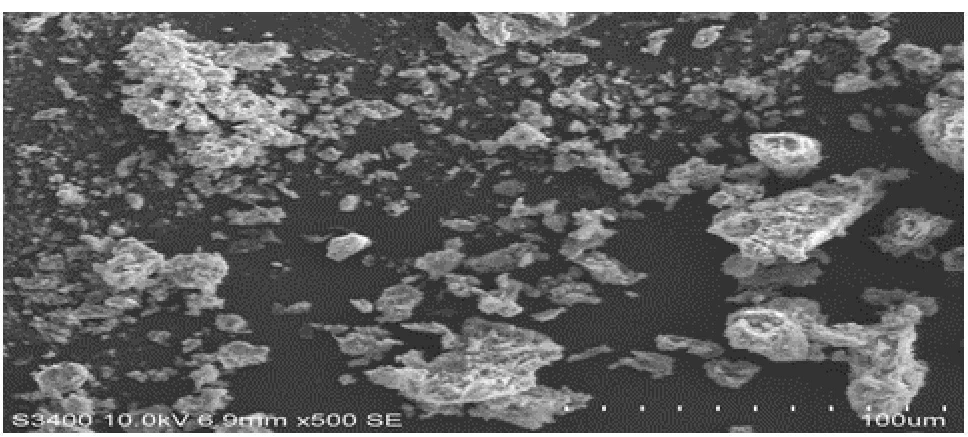


Figure 30: SEM Scanning picture of MC4.

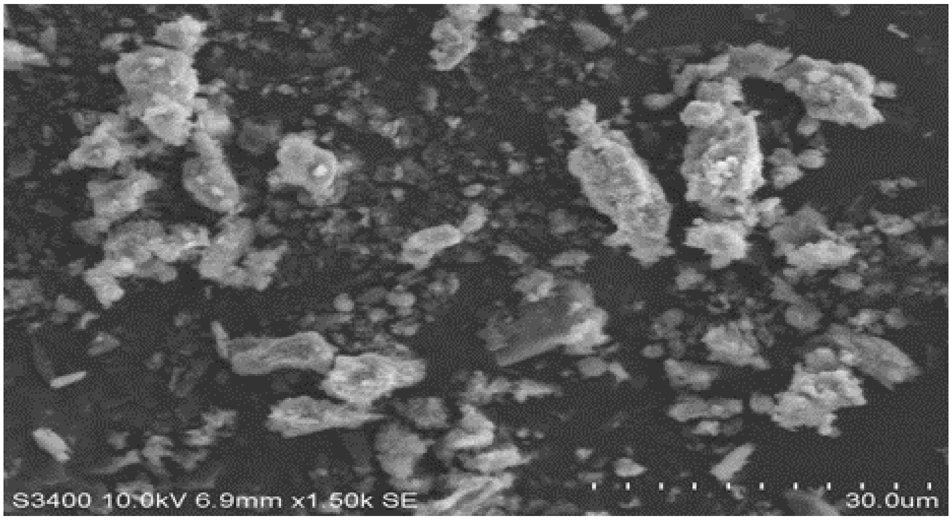


Figure 31: SEM Scanning picture of MC 5.

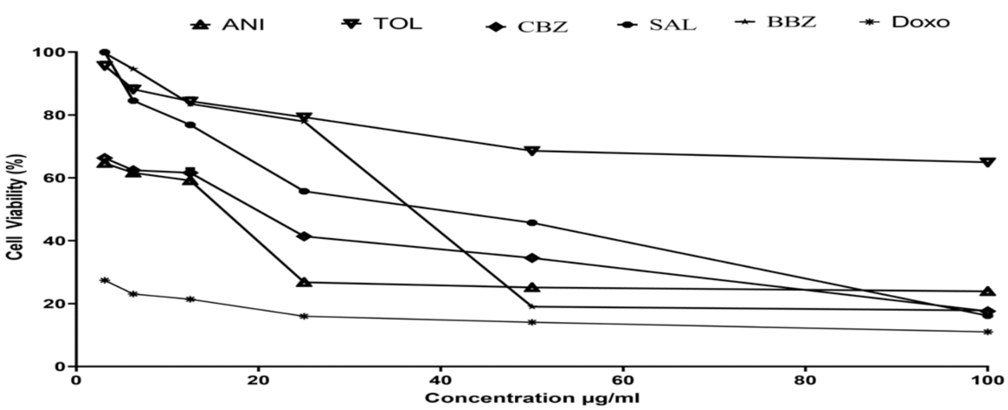


Figure 32: Cell viability study of organometal compounds vs Doxorubicin.

Table 10: Cytotoxic study results (IC_{50} values).

Sample codes	MCF-7	
	MEAN	SD
ANI	12.08	0.11
TOL	128.03	2.56
CBZ	15.96	0.26
SAL	34.67	0.72
BBZ	37.22	0.29
DOXORUBICIN	1.81	0.03

Table 11: Cell Viability study results of Organometal Compounds

Concentration µg/ml	ANI			TOL			CBZ		
100	23.83	22.89	24.95	64.73	65.10	65.10	17.26	18.00	17.07
50	24.39	25.14	25.89	68.86	68.11	68.86	34.33	35.08	34.15
25	26.83	27.02	26.45	80.11	79.17	78.61	40.90	41.45	41.84
12.5	58.72	59.66	59.10	85.55	83.30	84.24	63.04	60.41	61.35
6.25	61.73	61.35	61.73	89.49	87.43	87.62	63.60	61.73	61.91
3.125	65.10	63.98	64.92	95.12	94.93	97.00	65.85	66.98	66.04
Negative Control	100								
Cell Viability of MCF-7									
Concentration µg/ml	SAL			BBZ			Doxorubicin		
100	16.32	15.95	16.14	18.39	18.01	17.07	10.74	11.35	10.95
50	46.34	45.22	45.59	18.39	19.51	19.14	13.58	14.26	14.32
25	56.29	55.35	55.53	78.24	77.86	77.67	14.88	15.95	16.08
12.5	77.49	77.11	75.98	8349	83.30	83.86	21.15	21.55	21.42
6.25	85.37	84.80	83.49	94.00	95.50	94.37	22.64	23.04	23.45
3.125	99.81	99.81	100.38	98.31	100.00	100.75	27.23	27.36	27.64
Negative Control	100								

agents, however MC 1 and MC 5 are significantly good cytotoxic agents. However, further study is needed to justify this claim.

CONCLUSION

The organometallic compounds are often kinetically inert and can undergo multiple derivatization reactions. These characteristics makes them well-suited for conventional method of structure based drug design, including computer docking experiments, including those conducted for more traditional drug candidates. Despite the historical neglect of these organometallics in both academic and industrial drug research, an increasing number of emerging drug classes underscores the diverse possibilities that this field offers for synthetic medicinal chemistry. The ongoing progress of organometallic complexes towards clinical trials is expected to enhance their acceptance within the pharmaceutical industry, fostering further exploration and research into the development of metallo-drugs for anticancer purposes

In the current study, an attempt has been made to focus on highlighting the successful synthesis of various derivatives of Schiff base chelated with Aluminium (Al). These compounds have been characterized using spectral /analytical data such as IR, NMR, LCMS and metal analysis by ICPMS. Later, these organometallic compounds are evaluated for their anti-cancer potentials by *in vitro* method using selected cell cultures in the lab.Although additional studies are in progress and not yet disclosed to the public, we anticipate that this work represent a significant step towards developing new drug candidates in the field of medicinal organometallic chemistry. We envision that some of the most promising organometallic drug candidates discussed in this study may pave their way for the development of market for pharmaceuticals in the near future.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

TOL: Tolaldehyde (MC 1), ANI-Anisaldehyde (MC 2), **CBZ:** Chlorobenzaldehyde (MC-3), SAL-Salicylaldehyde (MC 4), Bromobenzaldehyde (MC 5), **IR:** Infrared spectroscopy; **NMR:** Nuclear magnetic resonance; **LCMS:** Liquid chromatography mass spectrometry; **SEM:** Scanning electron microscopy; **ICPMS:** Inductively coupled plasma Mass spectrometry.

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