

Docking, Protein Binding and Antimicrobial Activities of Coumarin Based Schiff Base and Mixed Ligand with 1, 10-Phen / 2, 2-Bipy Complexes

S. Sujarani¹, A. Ramu²

Assistant Professor, Department of chemistry, Parvathy's Arts and Science College, Dindigul, India¹

Professor & Head, Department of chemistry, School of Chemistry, Madurai Kamaraj University, Madurai, India²

ABSTRACT: The present study deals with anti-HIV, anti-cancer, anti-inflammatory important Fe (III)/Ru (III) Schiff base chelates. The complexes containing Fe (III)/Ru (III) ions were synthesized by using o-amino phenol / 2-aminothiophenol and 7-hydroxy coumarin. The ligand and complexes were characterized by analytical and spectral techniques. The spectral data confirm the ligand acts as a neutral bidentate Schiff base, coordinating through azomethine nitrogen and oxygen atom of hydroxyl/thiol group. The interaction studies of these complexes with BSA have also been performed by using spectral techniques collectively indicated with metal complexes. The microbial activity of the ligand and metal complexes using *Staphylococcus aureus*, *Escherichia Coli*, *Pseudomonas* and *Aspergillus niger* showed their enhanced inhibitory effect on their cell growth.

KEYWORDS: Schiff base; Protein binding; microbial activity, docking studies

I. INTRODUCTION

Environmental conditions and seasonal changes could influence the incidence of coumarin in varied parts of the plant. The function of coumarin is far from clear, although suggestions include plant growth regulators, bacteriostats, fungistats and even waste products.¹ Biosynthesis of coumarin is reviewed by Bourgaud et al.,² There are types of coumarin found in nature due to various permutations brought about by substitutions and conjugations; however, the most of the pharmacological and biochemical studies have been done on coumarin itself and on its primary metabolite, 7-hydroxycoumarin in man.³ Some of this earlier pharmacological work on coumarin has been reviewed,⁴ and other more comprehensive reviews^{3, 5-6} deal with the occurrence, chemistry and biochemical properties of both simple and more complex natural coumarin. Many researches on the biological activities of resveratrol have been reported including antioxidation,⁷ antiplatelet aggregation,⁸ cardioprotective activity,⁹ antitumor activity,¹⁰ anti-obesity and anti-diabetic activity.¹¹ One of the most striking biological activities of RV, which has been extensively investigated, is its antitumor property and it was discovered as a promising cancer chemo preventive agent on account of its outstanding inhibition on cellular events associated with cancer initiation, promotion and progression.¹² It has been documented that RV can modulate various signal transduction pathways resulting in the prevention of the carcinogenesis from diverse aspects. Several transcription factors such as NF-J B, AP-1, cyclooxygenase and kinases can be targeted by RV.¹³ However, its low bioavailability and rapid clearance from the circulation restrict it to behaving as an antitumor drug. Interaction studies by using Bovine serum albumin (BSA) is highly stable and comparatively cheap, (BSA) has the 80% structural similarity with HSA, BSA has been used as model by many group of researchers.¹⁴⁻¹⁹ Though BSA is a dietary protein, the most important function of BSA is transportation.¹⁹⁻²² This heart shaped protein, BSA is composed of a single chain of 583 amino acid residues and can be divided into three homologous domains, I-III²³ and each domain is made up of two sub domains, A and B, having unique binding properties.²⁴ BSA has two tryptophan residues; Trp-134 is available for the interaction with the binding molecules such

as drugs.²⁵ The emission property of Trp-134 and Trp-212 depends on the microenvironment of the protein. In this study, we report the synthesis, characterization and the binding properties of Fe (III) / Ru (III) complexes with BSA. This study has been carried out by UV-Vis, fluorescence spectroscopy, circular dichroism measurement. The aim of this work is to explore the interaction of Fe (III) / Ru (III) complexes with protein specifically aiming at the conformational changes of BSA. The obtained results show that the Fe(III)/Ru(III) complexes disturb the tertiary structure of BSA with loss of α -helix stability.

II. MATERIAL AND METHODS

All chemicals and solvents used in this study were of AR grade. O-amino phenol/2-amino thiophenol and 7-hydroxy coumarin (Sigma Aldrich), transition metal ions [Ferric (III) chloride (Merck) and Ruthenium(III) chloride (Sigma Aldrich), Bovine serum albumin (Sigma Aldrich), Tris-hydrochloride (SRL) and sodium chloride (SRL) were used as such without further purification.

Elemental analyses (C, H & N) were performed using an Elementary Vario EL elemental analyzer CHNS Mode. Metal contents were determined volumetrically by titration against standard EDTA solution after complete decomposition of their complexes with concentrated nitric acid. The chlorine content was determined by Volhard test. Molar conductivities of the metal complexes were determined in DMSO ($\sim 10^{-2}$ M) at room temperature using an EI Model 611E digital conductivity meter. The magnetic susceptibilities of complexes were determined on Gouy balance, and the diamagnetic corrections were made by Pascal's constant and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ was used as a calibrant. Nuclear magnetic resonance spectroscopic measurements were made on a Perkin-Elmer 300 MHz spectrometer. Deuterated organic solvents along with tetramethylsilane (TMS) as the internal standard were used. UV-Vis spectral measurements for the present complexes were made in DMSO solution using JASCO double beam recording spectrophotometer in the range 190–1100 nm. The infrared spectra of all complexes as well as ligands were recorded using KBr pellets on a JASCO FT-IR 410 double beam infrared spectrophotometer in the range of 400–4000 cm^{-1} . Cyclic voltammetric measurements were carried out on a Bio-Analytical System (BAS) CV-50W model electrochemical analyzer. The three electrodes cell comprising of a reference Ag/AgCl, counter electrode as platinum wire and working glassy carbon (GC) electrodes with surface area of 0.07 cm^2 were used. The GC was polished with 0.3 and 0.005 mm alumina before each experiment and if necessary the electrode was sonicated in distilled water for 10 min. Dissolved oxygen was removed by purging pure nitrogen gas into the solution for about 15 min before each experiment. A cyclic voltammogram has been recorded for a blank solution to check the purity of the supporting electrolyte and the solvent.

2.1. Protein Interaction studies

2.1.1 BSA interaction studies

All experiments involving BSA were performed in 50mM NaCl/Tris-HCl buffer solution (pH 7.4). BSA protein and the metal (III) complexes in NaCl/Tris-HCl buffer solution were used for analysis. For UV absorption, a 5mL solution of BSA (10 μM) was titrated with various concentrations of the complex. Equal solutions of complex were added to the reference solutions to eliminate the absorbance of the metal(III) complex itself. The quenching of the tryptophan fluorescence of BSA was studied at varying concentrations of the metal(III) complexes (quencher). The fluorescence spectra were recorded for BSA at an excitation wavelength of 285 nm and an emission wavelength of 347 nm in a fluorometer after addition of the quencher.

2.1.2. CD spectra

CD spectra of BSA in presence and absence of all the complexes were recorded on a JASCO J-810 (163–900 nm) spectropolarimeter using a quartz cuvette of 1 mm with optical path length at increasing complex/BSA ratio ($r = 0.01$ – 0.04). Each sample was scanned in the range of 220–320 nm. Each CD spectrum recorded was the average of at least four accumulations scanned at a speed of 100 nm min^{-1} and a 1s response time, from which the buffer back ground had been subtracted [$\text{BSA}] = 100 \mu\text{M}$].

2.1.3. SDS - PAGE- Analysis

The samples were treated with 1 µg of bovine serum albumin and incubated for 30 minutes at 37 °C. After incubation samples were resolved on polyacrylamide gel electrophoresis (SDS- PAGE) (Laemmli 1970). The gel was stained with Coomassie brilliant blue R-250. The binding property of the complexes with BSA was determined by comparison with the mobility of protein molecular weight markers (Fermentas, Opelstrasse, Germany).

2.2. Biological activity

2.2.1. Microbial activity of ligand and complexes

The synthesized ligand and its complexes were tested for their *in vitro* antimicrobial activity against the bacteria *Staphylococcus aureus*, *streptococcus* and *Escherichia coli*, *Klebsiella pneumonia*, using agar well diffusion method Luria Bertani medium was used for testing antibacterial activity. The stock solutions (10^{-2} mol L⁻¹) of the compounds were prepared in DMSO and the zone of inhibition values of the compound was determined. For determination of zone of inhibition, the respective medium was poured into the petriplates and allowed to solidify at room temperature. Wells were made on the solidified medium and the serially diluted were added on to the wells and allowed to diffuse into the wells. The indicator organisms were overlaid on to the agar medium and the plates were incubated for 37°C for 48 h. After incubation the zone of inhibition by the compound were measured and zone of inhibition was determined.

2.3. Docking Studies

2.3.1. Computational Methods:

Docking simulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method. Initial position, orientation, and torsions of the ligand molecules were set randomly. Each docking experiment was derived from 10 different runs that were set to terminate after a maximum of 250000 energy evaluations. The population size was set to 150. During the search, a translational step of 0.2 Å, and quaternion and torsion steps of 5 were applied.

2.4.1. Synthesis of ligand

(0.98g, 0.005M) of 2-hydroxy aniline / 2-aminothiophenol and (1.14g, 0.005M) of 7-hydroxy coumarin was dissolved in ethanol (25ml). The reaction mixture was refluxed in water bath at 60°C for 6 h until the yellow color homogeneous liquid solution was obtained and the completion of the reaction was monitored by TLC. The solid was washed 2 to 3 times with ethanol, evaporated to dryness and then recrystallised by ethanol. (85%) (Scheme.1)

2.4.2. Synthesis of complex

The present metal complexes were prepared by mixing of 0.01M of corresponding transition metal chloride in ethanol with 0.01M of the Schiff's base and 0.01M of phen/bipy in water. The reaction mixture was allowed to heat at 60°C with stirring at 6 h. Then it was allowed to cool to room temperature. The solid complexes were filtered, washed with ethanol, recrystallised from ethanol and dried in vacuum.(Scheme.2)

III. RESULT AND DISCUSSION

Elemental analysis data and physical characteristics of thiosemicarbazide Schiff's base ligand and complexes were summarized in Table S1 (Supplementary data file). The observed very low molar conductance of the complex in DMSO (10^{-2} M) solution at room temperature was consistent with non-electrolyte nature of the complexes.

3.1. ¹H NMR spectra of ligands

The ¹H NMR spectra of synthesized ligands showed the specific NMR signals on characterization of ligand Fig S1(a)(Supplementary data file). Signals of the aromatic protons lie in the range of 6 to 7.6 ppm. The presence of resonating signal at δ 3.4 and 10.5 ppm are accounted as OH protons.

3.2. ¹³C NMR spectra

The ¹³C NMR Fig S1(b) (Supplementary data file) spectrum consists of sharp signals at δ 102 – 158 ppm may be attributed to the phenyl carbon atoms and the signals C=N carbon assigned at δ 161 ppm and C-OH carbon assigned at δ 160 ppm.

3.3. IR spectra

The IR spectral data (table.S2) (Supplementary data file) provide valuable information regarding the coordination sites of the aldimine moiety, the bands around at 1597 cm⁻¹ obtained for ligand L, assigned as γ (C=N) vibrations.²⁶ These vibrations around were shifted to 1614 cm⁻¹ after complexation, due to an increase of bond order on coordination.²⁷ The IR band assignments of metal complexes exhibit broad bands in the range of 3298 cm⁻¹ indicating the water molecules coordinating.²⁸ New bands, which are not found in the ligand spectrum, appeared around 534 cm⁻¹, however have seen these bands at 470 cm⁻¹ corresponding to γ (M-N)^{29,30} and γ (M-O) vibrations, resulting support the involvement of N and O coordination's with metal centre³¹⁻³³ represented in Fig S2(a-f) (Supplementary data file).

3. 4. Electronic spectra

The electronic spectra (table S3) (Supplementary data file) and Fig S3 (Supplementary data file) of UV absorbance at 45,454 and 30,959 cm⁻¹ of ligand may be due to the characteristic π - π^* and n- π^* transitions of phenyl and imine groups respectively.^{34,35} The Fe (III) complex exhibits bands around 41,322cm⁻¹, 30,864 cm⁻¹. The high spin complex around 17,761 cm⁻¹ nm is assigned to ⁶A_{1g} → ⁴T_{2g}(G)³⁶ transition suggesting octahedral geometry which is confirmed by the magnetic moment value of 5.82 BM.³⁷ The electronic spectral data in of the Ru(III) complex is octahedral nature. In the six coordinate Ru(III) complex charge transfer transition often occurs at relatively low energy. Magnetic moment of the Ru(III) complex is lower than that of expected for Ru(III) low spin octahedral complex,^{38,39} which might be due to the magnetic interaction between Ru atoms in bridged complex.

3.5. Cyclic Voltammetry

Electrochemical characteristics of Fe(III) complexes, undertaken for this study, by cyclic voltammetry and the experimental results are summarized in table S4 and shown in Fig S4 (Supplementary data file). The cyclic voltammetric centers for the electrochemical reduction of the studied Ru(III) complexes display a redox couple in the range from 1200mV to -1200mV. Which may be attributed to the reduction of metal centers i.e., one electron quasi-reversible transfer process with the reduction peak at E_pc -666 mV and the corresponding oxidation peak E_pa -186 mV and $\Delta E_p = -480$ mV scanning rate 100mV/S. This study suggests chemical reversibility with Fe(III)/(II).⁴⁰

IV. INTERACTION OF BSA

4.1. Absorption studies

Interactions with the bovine serum albumins have been inferred from the changes in the absorption spectra (in the range 190–600 nm) on gradual addition of BSA at 298 K (Table.1. and Fig.1). The spectral changes acquired for BSA. Hyperchromism with small red shift has been detected. A change in the absorption spectra with a prominent support of interaction with BSA.

Table.1.Ligand-based absorption spectral properties of Fe(III) and Ru(III) complexes, bound^a to BSA.

Complexes	λ_{max} (nm)	Blue shift $\Delta\lambda$ (nm)	Binding constant K_b (M ⁻¹) $\times 10^4$
(L)Fe	437	1	0.12
(L ₁)Fe	323	1	4.15
(L)Fe-phen	505	1	0.15
(L ₁)Fe-phen	509	1	1.03
(L)Fe-bipy	508	1	0.09

(L ₁)Fe-bipy	521	2	1.16
(L)Ru	215	3	5.99
(L ₁)Ru	322	1	1.66
(L)Ru-phen	323	1	0.72
(L ₁)Ru-phen	263	1	4.09
(L)Ru-bipy	288	1	0.97
(L ₁)Ru-bipy	287	1	9.04

^aMeasurements made at different R values, where $R = \frac{[BSA]}{[complex]}$ concentrations of solutions of Fe(III) and Ru(III) complexes in pH 7.4 in 10% DMSO–buffer solutions.

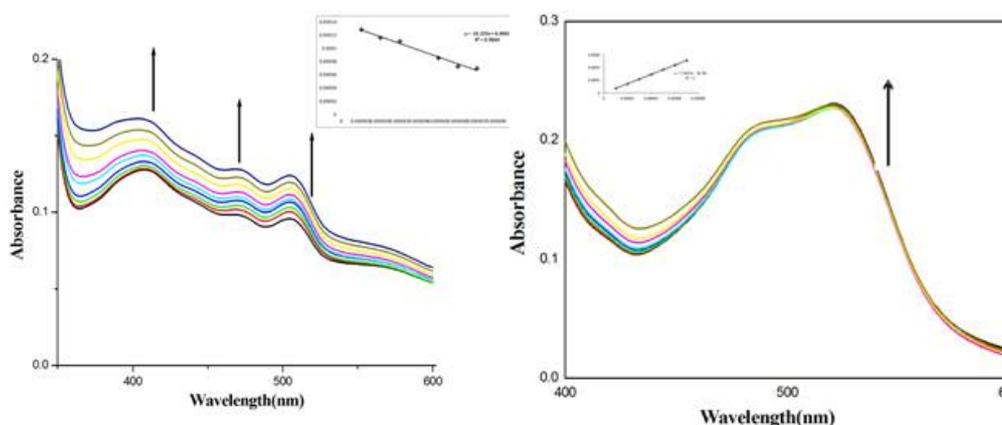


Fig.1. Absorption spectra of complex (a) (L)Ru-bipy and (b) (L₁)Fe-bipy (1.0×10^{-5} M), in Tris–HCl buffer pH 7.4 in the absence ($R = 0$) and presence ($R = 0.1, 0.2, 0.3, \dots, 0.8$) of increasing amounts of DNA. $R = \frac{[BSA]}{[complex]}$.

Arrow mark indicates the absorbance changes upon increasing DNA concentration and binding constant plot

4.2. Fluorescence studies

In order to confirm the interaction between Ru(III) complexes and BSA, luminescence titrations are also carried out for the same sample solutions. The emission titration results show that the emission intensity of the Ru(III) complexes is quenched with slight blue shift, 5–6 nm, in the presence of BSA. As a sample, results of the emission titration of complex 1a with BSA are illustrated in Fig. 2. Luminescence quenching refers to any process with a decrease of the luminescence intensity from a fluorophore due to a variety of molecular interactions⁴¹. These excited state reactions include molecular rearrangements, energy and electron transfer, ground state complex formation, and collisional quenching. Quenching can occur by different mechanisms, which are usually classified as dynamic and static quenching, revealed that the interaction of Ru(III) complexes with BSA is stronger binding constant. From these results, we can conclude that the quenching of the luminescence intensity of Ru(III) complexes is due to the interaction between Ru(III) complexes and BSA.

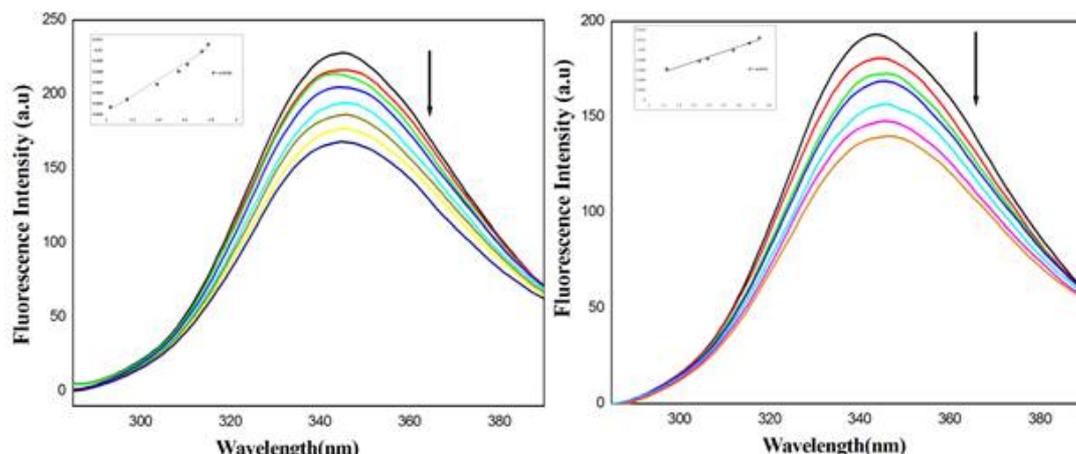


Fig.2. Emission spectra of complex BSA (1×10^{-4} M) in the presence of various concentrations of (a) (L)Ru-bipy and (b) (L)Ru-bipy: (0, 10, 20, 30, 40, 50, 60,) μ M, respectively. Excitation maximum = 285 nm.

4.2. CD studies

CD measurements provide insights about folding and unfolding of serum albumins induced by the ligand binding interactions. It has been found that binding to BSA causes a reduction of α -helix of the protein secondary structure from 68.4% (free BSA) to 67.55% ((L) Fe-bipy-BSA) binding. Such results suggest a partial protein unfolding for (L) Fe-bipy with BSA binding interactions but no significant conformational changes in the secondary and tertiary structures have been noted. For serum albumins (10 μ M), changes in the CD spectra for the secondary and tertiary structure have been noted (2 μ M) but such changes are much greater for BSA. It has been found that binding to BSA causes a reduction of α -helix of the protein secondary structure from 68.4% (free BSA) to 64.83% ((L)Ruphen – BSA) binding.⁴² Such results suggest a protein folding for (L)Ru –BSA binding interactions,⁴³ but significant conformational changes in the secondary and tertiary structures have been noted and shown in Fig.3.

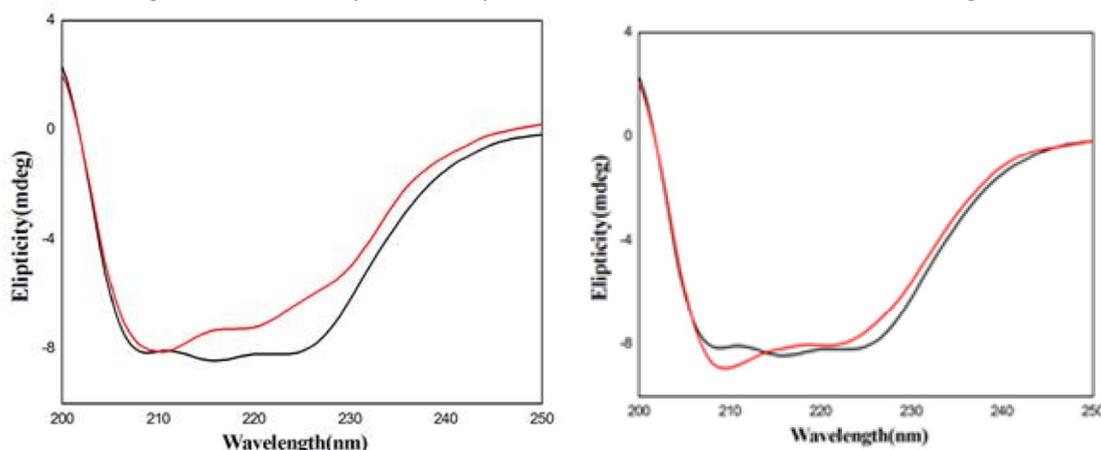


Fig.3. Circular dichroism spectra of BSA in the absence ($r = 0$) and in presence of complexes (a) (L)Ru-phen and (b) (L)Ru-bipy ($r = 0$ and 0.01); [BSA] = 100 μ M. Cell path length = 1 mm.

4.3. SDS- PAGE- Analysis

The ability of Ru(III) complexes to cleave BSA in the presence of white fluorescence light at 37 °C for 6 h was studied and the products was analyzed by 10% SDS-PAGE (Fig. 4). The Ru(III) showed cleavage activity. Interestingly, in the case of Ru(III) complexes one fragment of molecular weight (Mw) 72 kDa was observed in protein fragment. These experiments clearly demonstrate that Ru(III) complexes are more active.

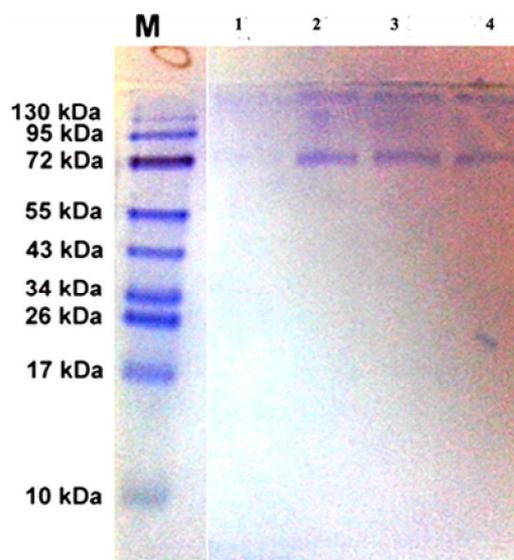


Fig.4. BSA cleavage at 37 °C with incubation for 6 h

Lane M: Marker

Lane 1: (L)Ru-phen 4 × 10⁻⁴ M

Lane 2: (L)Ru-phen 2 × 10⁻⁴ M

Lane 3: (L₁)Ru-phen 4 × 10⁻⁴ M

Lane 4: (L₁)Ru-phen 2 × 10⁻⁴ M

4.4. Antibacterial activity

Antibacterial activity of the ligand and its complexes has been carried out against the bacteria strains. A comparative study of zone of inhibition values of the Schiff base L and L₁ and their complexes indicate that the metal complexes exhibit higher antibacterial activity than the free ligands. It has been observed from the results that the metal complexes have higher antibacterial activity than free ligands. This is probably due to the greater lipophilic nature of the complexes. Such increased activity of the metal chelates could be explained on the basis of chelation theory. According to this concept, the cell favors the passage of only the lipid-soluble materials due to which lipid solubility are an important factor, which controls the antimicrobial activity. On chelation the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π electrons over the whole chelate ring and enhances lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membranes and blocking of the metal binding sites in the enzymes of microorganisms. These complexes also disturb the respiration process of the cell, thereby blocking the synthesis of the protein that inhibits the growth of the organism. Furthermore, the mode of action of the compounds may involve formation of at the C=N group with the active centers of cell constituents, resulting in an interference (Table.2) and microbial activity shown in Fig.5.

Table.2. Biological screening data for ligand and complexes

Compound	Zone of Inhibition (mm) <i>Staphylococcus aureus</i>	Zone of Inhibition (mm) <i>Sterptococcus</i>	Zone of Inhibition (mm) <i>E.Coli</i>	Zone of Inhibition (mm) <i>neumonia</i>
L	10	8	12	11
L ₁	12	10	15	14
(L)Fe	13	15	14	16
(L ₁)Fe	14	12	17	18
(L)Fe-phen	15	16	17	18
(L ₁)Fe-phen	16	14	18	20
(L)Fe-bipy	16	18	19	20

(L1)Fe-bipy	18	22	24	27
(L)Ru	12	14	16	15
(L1)Ru	13	15	18	17
(L)Ru-phen	15	11	17	19
(L1)Ru-phen	18	13	19	21
(L)Ru-bipy	13	14	16	20
(L1)Ru-bipy	15	17	18	22

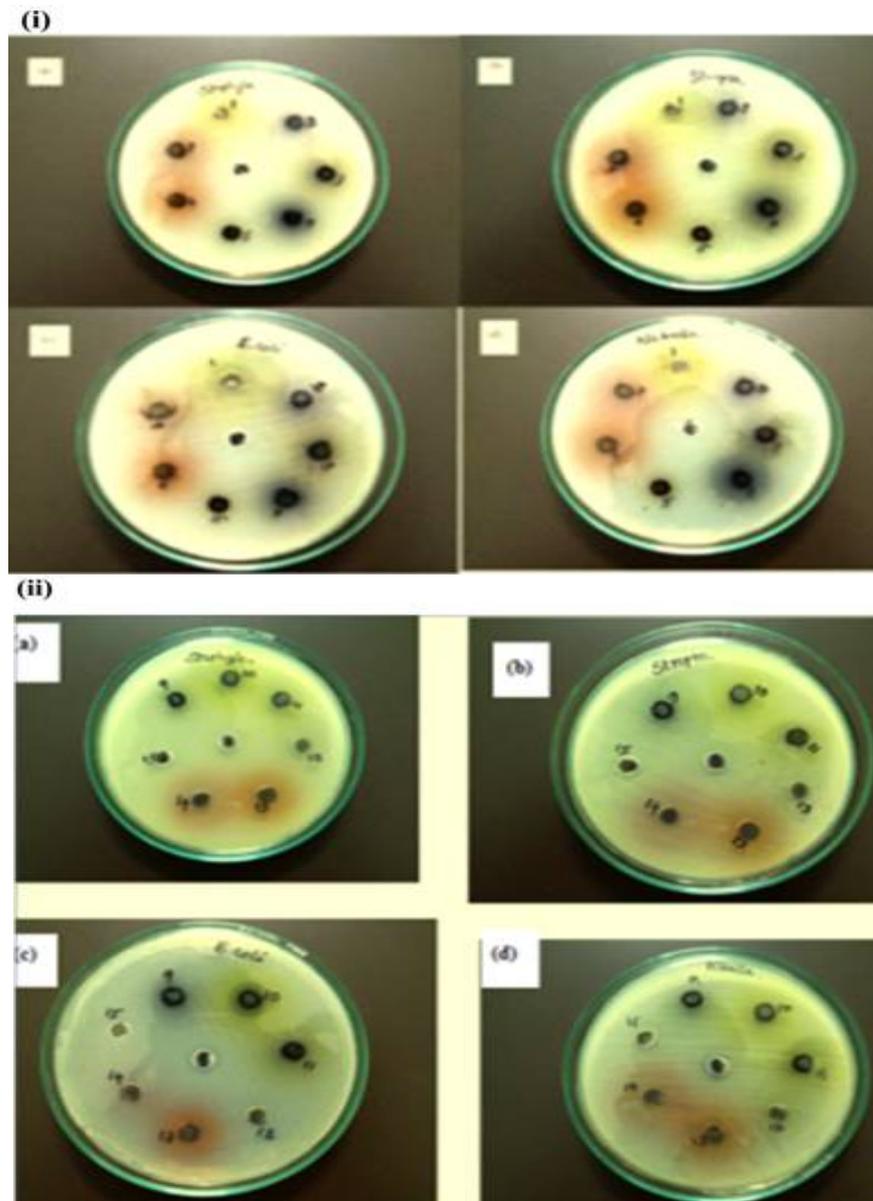


Fig.5(i). L and Complexes against the gram positive (a) *Staphylococcus aureus* (b) *Streptococcus* and gram negative (c) *Escherichia Coli* (d) *Klebsiella pneumonia*

Fig.5(ii) L₁ and complexes against the gram positive (a) *Staphylococcus aureus* (b) *Streptococcus* and gram negative (c) *Escherichia Coli* (d) *Klebsiella pneumonia*

4.5. Docking studies

The synthetic route used to synthesize title compounds is outlined in Scheme 1. L and L1 prepared by treatment of corresponding 2-hydroxy aniline / 2-aminothiophenol with 7-hydroxy coumarin in the presence of ethanol. The structure of synthesized compound was assigned on the basis of their spectral studies. In the present study, we constructed a protein-ligands complex model with an X-ray crystal structure (PDB code 3F7Z; Fig 6) and the ligands were observed in crystal complex structures using MMFF94 simulation and by Gasteiger partial charges to gain better enrichment in virtual screening. Docking simulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method (Solis and Wets, 1981). Initial position, orientation, and torsions of the ligand molecules were set randomly. Each docking experiment was derived from 10 different runs that were set to terminate after a maximum of 250000 energy evaluations. The population size was set to 150. During the search, a translational step of 0.2 Å, and quaternion and torsion steps of 5 were applied. Interestingly, docking results reveal that all the compounds inside GSK3-β protein is outlined by different amino acids and the hydrophobic pocket is comprised of VAL 214 & ILE 228. Small molecules are bound to human serum albumin by four binding modes; Hydrogen bonds, Van der Waals, electrostatic & hydrophobic interactions. The result gives the total energy of four binding modes & is shown in table 3. Calculated free energy of binding for compound in the inhibitor binding site (IBS) were -5.15 and -6.01 kcal/mol in the best pose. The HB plot of the L and L1 show the interaction of protein with the different amino acid residues. From our results, we presumed that compound L and L1 are anchored in to binding site SER 118 and THR 157 while the confirmation stability is brought about by other interactions in table 4.44-47

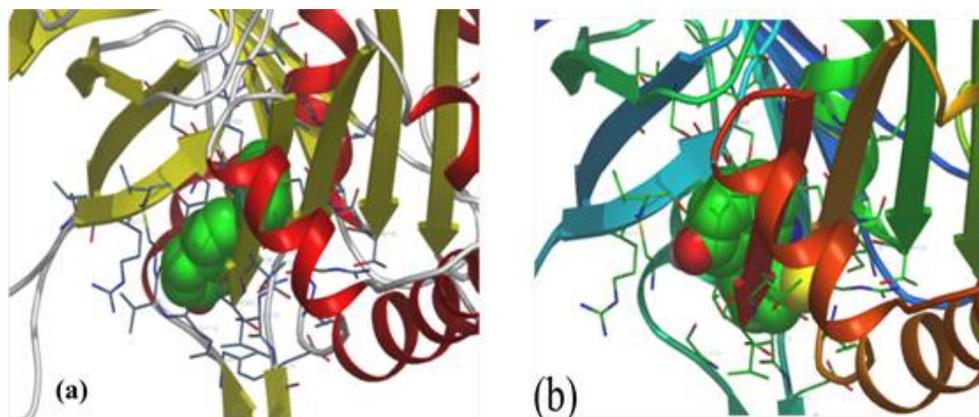


Fig.6. Visualization of the conformation of (a) L and (b) L₁ (an in built application of Molecular docking server) BSA

V. CONCLUSIONS

In summary, the complexes of Fe(III) and Ru(III) have been synthesized and characterized by UV-Vis, IR, NMR, ESI-Mass, EPR and cyclic voltammetric techniques. The biological interactions between the complexes and CT-DNA and bovine serum albumin (BSA) have been investigated using spectral techniques. The results obtained collectively that all the complexes showed strongly interaction with CT-DNA, may be groove binding mode. The interaction characterization is supported by the following findings:

- Schiff base ligand and their Ru(III),Fe(III) metal complexes have been synthesized and used for the study.
- The biological interactions between the complexes with bovine serum albumin (BSA) have been investigated using spectral techniques.
- The results obtained collectively by all the complexes showed strongly interaction with BSA.

The experimental results exhibited by all the ligands and complexes undertaken for this study against the gram positive (*Staphylococcus aureus*, *Streptococcus*) and gram negative (*Escherichia Coli*, *Klebsiella pneumonia*) are very promising when compared with those of the standards.

ACKNOWLEDGEMENT

We gratefully acknowledge the financial support received from JRF meritorious fellowship Ref. No. F4-1/2006(BSR)/7-119/2007(BSR) UGC, New Delhi for carrying out this research work. Author also thankful to the Chairperson, School of Chemistry, Madurai Kamaraj University for providing the necessary facilities required carry out this work. We thank Dr. P. Gunasekaran, Senior Professor, and Dr. J. Rajendhran, Department of Genetics, School of Biological Sciences, Madurai Kamaraj University for their help in the biological studies. Finally I thank Parvathy's Arts and Science College, Management and Principal Dr.G.Sukumar.

REFERENCES

- [1] D. Bogdal, *Journal of Chemical Research, Synopses*, 8 (1998) 468–469, doi:10.1039/a801724g
- [2] F. Bourgaud, A. Hehn, R. Larbat et al., *Phytochemistry Reviews*, 5, (2006) 293–308. DOI:10.1007/s11101-006-9040-2
- [3] B. G. Lake, *Food and Chemical Toxicology*, 37, (1999) 423–453. doi.org/10.1016/S0278-6915(99)00010-1.
- [4] D. Egan, R. O'Kennedy, E. Moran, D. Cox, E. Prosser, and R. D. Thornes, *Drug Metabolism Reviews*, 22, (1990) 503–529. doi: 10.3109/03602539008991449
- [5] M. E. Marshall, J. L. Mohler, K. Edmonds et al., *Journal of Cancer Research and Clinical Oncology*, 120, (1994) supplement, S39–S42. DOI 10.1007/BF01377124
- [6] R. D. H. Murray, in *Progress in the Chemistry of Organic Natural Products*, Springer, New York, NY, USA, (1997) 2–105.
- [7] Fauconneau B, Waffo-Teguou P, Huguet F, Barrier L, Decendit A, Merillon JM (1997). *Life Sci* 61:2103–2110. doi: 10.1016/S0024-3205(97)00883-7.
- [8] Pace-Asciak CR, Hanh S, Diamandis EP, Soleas G, Goldberg DM, *Clin Chim Acta* 235 (1995) 207–219. [http://dx.doi.org/10.1016/0009-8981\(95\)06045-1](http://dx.doi.org/10.1016/0009-8981(95)06045-1)
- [9] Mokni M, Limam F, Elkahoui S, Amri M, Aouani E (2007) *Arch Biochem Biophys* 457, 1–6. <http://dx.doi.org/10.1016/j.abb.2006.10.015>
- [10] Bishayee A, Politis T, Darvesh AS (2010) *Cancer Treat Rev* 36, 43–53. doi: 10.1016/j.ctrv.2009.10.002
- [11] Szkudelska K, Szkudelski T (2010) *Eur J Pharmacol* 635, 1–8. doi: 10.1016/j.ejphar.2010.02.054
- [12] Jang M, Cai L, Udeani GO, Slowing KV, Thomas CF, Beecher CW, Fong HH, Farnsworth NR, Kinghorn AD, Mehta RG, Moon RC, Pezzuto JM (1997) *Science* 275, 218–220
- [13] Athar M, Back JH, Kopelovich L, Bickers DR, Kim AL (2009) *Arch Biochem Biophys* 486, 95–102. doi: 10.1016/j.abb.2009.01.018
- [14] T. Peters Jr All about albumin. *biochemistry, genetics and medical applications Academic Press Orlando, FL*, (1996) 432.
- [15] B.K. Paul, A. Samanta, N. Guchhait, *J. Phys. Chem. B*, 114 (2010) 6183–6196. DOI: 10.1021/jp100004t.
- [16] D.C. Carter, J.X. Ho, Structure of serum albumin, *Adv Protein Chem*, 45 (1994)153–203.
- [17] X.M. HE, C.D. CARTER, *NATURE*, 358 (1992) 209–215. DOI:10.1038/358209A0
- [18] S. MAHANTA, R.B. SINGH, N. GUCHHAIT, *J. FLUORESC*, 19 (2009) 291–302. DOI: 10.1007/s10895-008-0415-1
- [19] R.B. Singh, S. Mahanta, A. Bagchi, N. Guchhait, *Photochem Photobiol. Sci.*, 8 (2009)101–110. DOI: 10.1039/B814050B
- [20] R.B. Singh, S. Mahanta, N. Guchhait, *Spectrochim Acta, Part A*, 72 (2009)1103–1111. DOI: 10.1016/j.saa.2009.01.011
- [21] P. Banerjee, S. Pramanik, A. Sarkar, S.C. Bhattacharya, *J. Phys. Chem B*, 113 (2009) 11429–11436. DOI: 10.1021/jp4090553
- [22] D. Zhong, A. Douhal, A.H. Zewail, Proceedings of the National Academy Sciences of the United States of America, 97 (2000) 14056–14061. Doi: 10.1073/pnas.250491297
- [23] O.J.M. Bos, J.F.A. Labro, M.J.E. Ficher, J. Witling, L.H.M. Janssen, *J Biol Chem*, 264 (1989) 953–959. [http://dx.doi.org/10.1016/0014-5793\(95\)01231-2](http://dx.doi.org/10.1016/0014-5793(95)01231-2)
- [24] T. Peters Jr, "Serum Albumin," *Advances in protein chemistry*. Academic, New York, 37 (1985) 161–245. [http://dx.doi.org/10.1016/S0065-3233\(08\)60065-0](http://dx.doi.org/10.1016/S0065-3233(08)60065-0)
- [25] D. Li, M. Zhu, C. Xu, B. Ji, *European Journal of Medicinal Chemistry*, 46 (2011) 588–599. <http://dx.doi.org/10.1016/j.ejmech.2010.11.038>
- [26] J. Jezowska & P. Lisowski, *Polyhedron*, 7 (1988) 337–343. [http://dx.doi.org/10.1016/S0277-5387\(00\)80480-5](http://dx.doi.org/10.1016/S0277-5387(00)80480-5)
- [27] J.M.Seco, M. Quiros, M.J.G. Garmendia, *Polyhedron*, 19 (2000)1005–1013. [http://dx.doi.org/10.1016/S0277-5387\(00\)00356-9](http://dx.doi.org/10.1016/S0277-5387(00)00356-9)
- [28] K. Nakamoto, *Infrared and Raman Spectra of inorganic and coordination comp Edition*, Wiley, New York, (1997) 79–82.
- [29] A. Jain, R. Goyal, D.D. Agarwal, *J. Inorganic Nuclear Chem*, 43 (1981) 2005–2009. [http://dx.doi.org/10.1016/0022-1902\(81\)80537-4](http://dx.doi.org/10.1016/0022-1902(81)80537-4)
- [30] A. Abragam, M.H.L. Pryc, *Proc Roy Soc., London*, 205 (1951)135.
- [31] J. Sanmartin, M.R. Bermejo, A.M.G. Deibe, C. Manejo, Lage, A.J.C Filho, *Polyhedron*, 19 (2000) 185–192. [http://dx.doi.org/10.1016/S0277-5387\(99\)00341-1](http://dx.doi.org/10.1016/S0277-5387(99)00341-1)
- [32] D.N. Sathyanarayana, *Electronic Absorption Spectroscopy and Related Techniques*, New Delhi Universities Press, (2001).
- [33] B. Bosnich, *J. Am Chem.Soc.*, 90 (1968) 627–632. doi: 10.1021/ja01005a012
- [34] R.S. Dowing and F.L.Urbach, *J.Am Chem. Soc.*, 91 (1969) 5977–5983. DOI: 10.1021/ja01050a700
- [35] Fahmideh Shabani, Lotf Ali, Saghat Foroush, Shahriar Ghammamy, *Bull. Chem. Soc.*, 24 (2010)193–199.
- [36] A. Kulkarni, S. Sangamesh Patil, Prema Badami, *Int. J. Electrochem. Sci.*, 94 (2009) 717–729.
- [37] A.B.P. Lever, *Electronic spectra of dn ions. In Inorganic Electronic Spectroscopy*, 2nd Ed.; Elsevier: New York, (1984) 376.
- [38] P. Viswanathamurthi, K. Natarajan, *Synth. React. Inorg. Met.-Org. Chem.* 28 (1998) 437–444.
- [39] J. Heinze, *Angew. Chem*, 23 (1984) 831–847. DOI: 10.1002/anie.198408313

International Journal of Innovative Research in Science, Engineering and Technology

An ISO 3297: 2007 Certified Organization

Volume 7, Special Issue 8, September 2018

International Conference on Emerging Trends in Science, Technology and Mathematics (ICETSTM-2018)"

22nd August 2018

Organized by

Department of Computer Science, Parvathy's Arts and Science College, Dindigul, Tamilnadu, India

- [40] B. Sengupta, P.K. Sengupta, *Biopolymers* 72(2003) 427-434. DOI: 10.1002/bip.10489
- [41] J.R. Lakowicz, G. Weber, *Biochemistry* 12 (1973) 4171-4179. DOI: 10.1021/bi00745a021
- [42] M. Gharagozlou, D.M. Boghaei, *Spectrochim. Acta Part A*, 71 (2008) 1617- 1622. <http://dx.doi.org/10.1016/j.saa.2008.06.027>
- [43] Elzbieta Budzisz *et al.*, *Inorg. Chem.* 45 (2006) 9688-9695. DOI: 10.1021/ic0601788
- [44] Z. Bikadi, E. Hazai, *J. Cheminf.*, (2009) 1-16.
- [45] T. A. Halgren, *Journal of Computational Chemistry*, 17(1998) 490-519. DOI: 10.1002/(SICI)1096-987X(199604)17:5/6<490::AID-JCC1>3.0.CO;2-P
- [46] G. M. Morris, D. S. Goodsell, *et al.*, *Journal of Computational Chemistry*, 19(1998)1639-1662. DOI: 10.1002/(SICI)1096-987X(19981115)19:14<1639::AID-JCC10>3.0.CO;2-B
- [47] F. J. Solis and R. J. B. Wets, *Mathematics of Operations Research*, 6 (1981)19-30. doi.org/10.1287/moor.6.1.19