



## Research Article

### ANTIMICROBIAL ACTIVITIES OF BIIMIDAZOLE BASED MIXED LIGAND RUTHENIUM(II) COMPLEXES

Mathiyalagan Kiruthika <sup>1</sup>, Rajendran Sivasankari <sup>1</sup>, Ramasamy Elayaperumal <sup>2</sup>, Chellamuthu Hariharan <sup>3</sup>, Periasamy Dharmalingam <sup>4\*</sup>

<sup>1</sup>Department of Chemistry, Government Arts College for Women, Salem, Tamil Nadu, India

<sup>2</sup>Department of Chemistry, J. J. College of Engineering and Technology, Tiruchirappalli, Tamil Nadu, India

<sup>3</sup>Department of Physics, Jamal Mohamed College, Trichy, Tamil Nadu, India

<sup>4</sup>Department of Chemistry, Urumu Dhanalakshmi College, Tiruchirappalli, Tamil Nadu, India

\*Corresponding Author Email: drpdharmalingamudc1@gmail.com

Article Received on: 01/07/16 Revised on: 20/07/16 Approved for publication: 02/08/16

DOI: 10.7897/2230-8407.07893

#### ABSTRACT

Ruthenium(II) complexes of the type  $[\text{Ru}(\text{bpy})_2(\text{L})](\text{PF}_6)_2$ , where L=4,5-bis(4-dimethylaminophenyl)-1H,1'H-2,2'-biimidazole (**1**) and 4,5-bis(4-fluorophenyl)-1H,1'H-2,2'-biimidazole (**2**) that combine the structure of bipyridine and substituted biimidazole derived from dimethylaminobenzil and fluorobenzil have been synthesized and characterized by elemental analyses and spectral (IR, UV-vis, EI-MS) techniques. The redox behavior of the complexes has been studied by cyclic and differential pulse voltammetry. The synthesized ligands and complexes have been tested for in vitro growth inhibitory activity against two Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*), two Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*), and two fungi (*Aspergillus niger* and *Candida albicans*). The antimicrobial activities of the complexes showed better activity compared to that of the ligands.

**Keywords:** Biimidazole, Ruthenium(II), antibacterial, antifungal, Gram-positive, Gram-negative.

#### INTRODUCTION

Though transition metals occupy many key positions in biological processes, metal-based drugs are traditionally undervalued by the pharmaceutical industry, which is dominated by organic chemistry. Nevertheless, a number of coordination compounds have been applied in the therapy of various diseases<sup>1-5</sup>. Ruthenium is a very good metal to be used in metal complex drugs considering its ability to mimic iron in binding to certain biological molecules<sup>6</sup>. Ruthenium compounds are regarded as promising alternatives to platinum compounds and offer many approaches to innovative metallopharmaceuticals, the compounds are known to be stable and to have predictable structures both in the solid state and in solution: tuning of ligand affinities and accompanied by a steadily increasing knowledge of the biological effects of ruthenium compounds<sup>7-9</sup>. Many ruthenium compounds are evaluated for clinical applications mostly for cancer treatment. Ru(II) and Ru(III) complexes having the similar ligand exchange rates compared to Pt(II) complex (cis-platin, carboplatin, etc.) which shown to be anticancer agents<sup>10-14</sup>. Ligand exchange is an important criterion when it comes to clinical applications. Very few molecules are able to reach the biological targets without being modified.

Dwyer and co-workers first illustrated the excellent antibacterial activity of the ruthenium(II) polypyridyl complexes against drug-sensitive strains<sup>15</sup>. However, these complexes were considerably less active against the corresponding current drug-resistant strains. Recently, inert ruthenium complexes containing heterocyclic ligands have been investigated as antimicrobial agents<sup>16-20</sup>. The unique properties of the ruthenium(II) polypyridyl complexes are that they do not change their

structure under physiological conditions and are stable in strong acids and bases. Keeping the above facts in mind, mononuclear ruthenium(II) complexes of type  $[\text{Ru}(\text{bpy})_2(\text{L})](\text{PF}_6)_2$  (where L=4,5-bis(4-dimethylaminophenyl)-1H,1'H-2,2'-biimidazole (**1**) and 4,5-bis(4-fluorophenyl)-1H,1'H-2,2'-biimidazole (**2**)) have been synthesized and characterized and the invitro antimicrobial activity of the compounds have been explored.

#### MATERIALS AND METHODS

Ruthenium chloride trihydrate, imidazole-2-carboxaldehyde, ammonium hexafluoro phosphate, 4,4'-difluorobenzil and 4,4'-bis(dimethylamino benzil) were purchased from Sigma-Aldrich. Acetic acid, ammonium acetate, methanol, acetonitrile and ethanol were purchased from SD Fine chemicals.

Absorption spectra were recorded on Shimadzu UV-160A UV-Visible spectrophotometer. Cyclic (CV) and differential pulse voltammetries (DPV) were performed by using CH instrument (USA) model CH-620 B electrochemical analyzer. A conventional three electrode system consisting of platinum disc as a working electrode, platinum wire as an auxiliary electrode and saturated calomel (SCE) as a reference electrode was used for the electrochemical measurements. 0.1 M tetrabutyl ammonium perchlorate (TBAP) was used as the supporting electrolyte for all the experiments. Elemental analyses were performed using Elementar Vario EL III at Sophisticated Test and Instrumentation Centre (STIC), Kerala. Positive ion electron ionization mass spectra of the complexes were obtained by using Thermo Finnigan LCQ 6000 advantage max ion trap mass spectrometer. IR spectra were recorded as KBr pellets in the

400 - 4000  $\text{cm}^{-1}$  region using a Shimadzu FT-IR 8000 spectrophotometer.

### Synthesis of Ligands

#### Synthesis of 4,5-bis(4-dimethylaminophenyl)-1H,1'H-2,2'-biimidazole (L1)

4,4'-bis(dimethylamino)benzil (0.2 g, 0.67 mmol), imidazole-2-carboxaldehyde (0.068 g, 0.71 mmol) and ammonium acetate (2 g, 25 mmol) were dissolved in 15 mL acetic acid and heated to reflux for 3 h. After cooling, cold water (10 mL) was added to the solution, during which light green precipitate was appeared. It was filtered and recrystallized using ethanol (Yield 0.13 g, 48 %). EI-MS:  $m/z$  373.5 (M+1)<sup>+</sup>. Anal. Calc. for  $\text{C}_{22}\text{H}_{24}\text{N}_6$ : C, 70.94; H, 6.49; N, 22.56. Found: C, 70.89; H, 6.46; N, 22.52. IR,  $\text{cm}^{-1}$ (KBr pellet) 3479, 3088, 1618, 1587, 1381.

#### Synthesis of 4,5-bis(4-fluorophenyl)-1H,1'H-2,2'-biimidazole (L2)

4,5-bis(4-fluorophenyl)-1H,1'H-2,2'-biimidazole was synthesized by using the same procedure described above by reacting imidazole-2-carbaldehyde (0.081 g, 0.85 mmol) with 4,4'-difluorobenzil (0.2 g, 0.81 mmol) and ammonium acetate (Yield 0.12 g, 44 %). EI-MS:  $m/z$  323.4 (M+1)<sup>+</sup>. Anal. Calc. for  $\text{C}_{18}\text{H}_{12}\text{F}_2\text{N}_4$ : C, 67.08; H, 3.75; N, 17.38. Found: C, 67.05; H, 3.71; N, 17.32. IR,  $\text{cm}^{-1}$  (KBr pellet) 3435, 3072, 1616, 1590, 1413.

### Synthesis of Complexes

#### Synthesis of $[\text{Ru}(\text{bpy})_2(\text{L1})](\text{PF}_6)_2$ (1).

A mixture of  $[\text{cis-Ru}(\text{bpy})_2\text{Cl}_2]\cdot 2\text{H}_2\text{O}^{21}$  (0.2 g, 0.38 mmol) and L1 (0.14 g, 0.38 mmol) was suspended in an ethanol/water solvent mixture (3/1, v/v). The mixture was refluxed under an inert atmosphere for 4 h while vigorous stirring was maintained. The reaction mixture was cooled to room temperature; the solvent was reduced under vacuum to one-third of its initial volume. A saturated aqueous solution of  $\text{NH}_4\text{PF}_6$  was added to precipitate  $[\text{Ru}(\text{bpy})_2(\text{L1})]^{2+}$  as its hexafluorophosphate salt. The product was filtered and washed with water ( $3 \times 10$  mL) and then purified by column chromatography on neutral alumina using acetonitrile/toluene (1.5/1, v/v) as an eluent. Yield: 0.2739 g, 67 %. Anal. Calc. for  $\text{C}_{42}\text{H}_{40}\text{F}_{12}\text{N}_{10}\text{P}_2\text{Ru}$ : C, 46.89; H, 3.75; N, 13.02. Found: C, 46.86; H, 3.70; N, 12.99. EI-MS:  $m/z$  1076.71 (M+1)<sup>+</sup>; IR,  $\text{cm}^{-1}$ (KBr pellet) 3429, 3097, 1589, 1379,

1247, 840, 765. UV-Visible  $\lambda_{\text{max}}$ , nm ( $\epsilon$ ,  $\text{M}^{-1}\text{cm}^{-1}$ ) 279(63740), 321(46680), 474(9220).

#### Synthesis of $[\text{Ru}(\text{bpy})_2(\text{L2})](\text{PF}_6)_2$ (2).

The synthesis and purification of compound 2 were similar to those of 1 using  $[\text{Ru}(\text{bpy})_2\text{Cl}_2]\cdot 2\text{H}_2\text{O}$  (0.2 g, 0.38 mmol) and L2 (0.12 g, 0.38 mmol). Yield: 0.2299 g, 59 %. Anal. Calc. for  $\text{C}_{38}\text{H}_{28}\text{F}_{14}\text{N}_8\text{P}_2\text{Ru}$ : C, 44.50; H, 2.75; N, 10.92. Found: C, 44.47; H, 2.71; N, 10.90. EI-MS:  $m/z$  1026.23 (M+1)<sup>+</sup>; IR,  $\text{cm}^{-1}$ (KBr pellet) 3394, 3074, 1666, 1598, 1415, 1232, 844, 759. UV-Visible  $\lambda_{\text{max}}$ , nm ( $\epsilon$ ,  $\text{M}^{-1}\text{cm}^{-1}$ ) 283(38140), 329(54040), 478(6040).

### Antimicrobial Assay

Test Microorganisms: Two Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*), two Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*), and two fungi (*Aspergillus niger* and *Candida albicans*) were used in the present study for evaluation of antimicrobial activity of the synthesized compounds. Medium used for the antimicrobial testing was Muller Hilton agar media and autoclaved at 15 lbs/in<sup>2</sup> for 15 minutes.

Antimicrobial Activity: Agar disc diffusion method was used to study the antimicrobial activity of the newly synthesized compounds<sup>22,23</sup>. For the evaluation of antimicrobial activity, the size of inoculum was adjusted to approximately 108 colony-forming units (cfu/mL) by suspending the culture in sterile distilled water. Petri dishes containing 20 mL of Muller Hilton agar medium were swabbed with a culture of the respective microbial strains and kept for 15 min for the absorption of culture. Sterile borer is used to create the wells (6mm in diameter), and we added 25, 50, 75 and 100  $\mu\text{L}$  solution of each compound of 25, 50, 75 and 100  $\mu\text{g}/\text{mL}$  concentration respectively reconstituted in the DMSO on the pre-inoculated plates. All the plates were incubated at 37°C for 24 hrs. Antimicrobial activity of all the synthesized compounds was determined by measuring the zone of inhibition around the wells. DMSO was used as a negative control, whereas Gentamycin was used as positive control. This procedure was performed in three replicate plates for each organism.

**Table 1: Electronic and electrochemical data of mononuclear Ruthenium(II) complexes in Acetonitrile solution at 25 ± 0.2 °C**

| Complex   | $\lambda_{\text{max}}$ , nm<br>( $\epsilon$ , $\text{M}^{-1}\text{cm}^{-1}$ ) | $E_{\text{pa}}$ (V) | $E_{\text{pc}}$ (V) | $\Delta E_{\text{p}}$ (mV) | $E_{1/2}$ $\text{Ru}^{\text{II}}/\text{Ru}^{\text{III}}$ vs SCE |         |
|---|---|---------------------|---------------------|----------------------------|---|---------|
|   |   |                     |                     |                            | CV (V)  | DPV (V) |
| $[\text{Ru}(\text{bpy})_2(\text{L1})](\text{PF}_6)_2$ | 474 (9220)<br>321(46680)<br>279(63940)  | +0.9095             | +0.8301             | 79                         | +0.8698   | +0.8687 |
| $[\text{Ru}(\text{bpy})_2(\text{L2})](\text{PF}_6)_2$ | 478(6040)<br>329(54040)<br>283(38140)   | 0.8770              | +0.8019             | 75                         | +0.8395   | +0.8311 |

**Table 2: Antibacterial activity of Ligands and their Ruthenium (II) complexes**

| Test Drug           | Zone of Inhibition (mm)       |                               |                               |                                |                               |                               |                               |                                |                               |                               |                               |                                |                               |                               |                               |                                |
|---------------------|-------------------------------|-------------------------------|-------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------------------|--------------------------------|
|                     | <i>S. aureus</i>              |                               |                               |                                | <i>B. Subtilis</i>            |                               |                               |                                | <i>E. coli</i>                |                               |                               |                                | <i>P. aeruginosa</i>          |                               |                               |                                |
|                     | 25<br>$\mu\text{g}/\text{mL}$ | 50<br>$\mu\text{g}/\text{mL}$ | 75<br>$\mu\text{g}/\text{mL}$ | 100<br>$\mu\text{g}/\text{mL}$ | 25<br>$\mu\text{g}/\text{mL}$ | 50<br>$\mu\text{g}/\text{mL}$ | 75<br>$\mu\text{g}/\text{mL}$ | 100<br>$\mu\text{g}/\text{mL}$ | 25<br>$\mu\text{g}/\text{mL}$ | 50<br>$\mu\text{g}/\text{mL}$ | 75<br>$\mu\text{g}/\text{mL}$ | 100<br>$\mu\text{g}/\text{mL}$ | 25<br>$\mu\text{g}/\text{mL}$ | 50<br>$\mu\text{g}/\text{mL}$ | 75<br>$\mu\text{g}/\text{mL}$ | 100<br>$\mu\text{g}/\text{mL}$ |
| L1                  | 10                            | 13                            | 16                            | 19                             | 12                            | 13                            | 16                            | 19                             | 9                             | 11                            | 13                            | 15                             | 9                             | 11                            | 15                            | 18                             |
| L2                  | 10                            | 12                            | 15                            | 18                             | 10                            | 12                            | 14                            | 16                             | 9                             | 12                            | 14                            | 16                             | 9                             | 11                            | 13                            | 15                             |
| 1                   | 18                            | 22                            | 24                            | 26                             | 15                            | 20                            | 24                            | 28                             | 16                            | 22                            | 25                            | 29                             | 10                            | 11                            | 13                            | 16                             |
| 2                   | 20                            | 23                            | 26                            | 29                             | 14                            | 18                            | 22                            | 26                             | 16                            | 20                            | 25                            | 28                             | 15                            | 17                            | 19                            | 21                             |
| Gentamycin Standard | -                             | -                             | -                             | 17                             | -                             | -                             | -                             | 18                             | -                             | -                             | 18                            | -                              | -                             | -                             | -                             | 18                             |

Note: Zone size less than 15 mm – Least active; 16 – 20 mm – moderately active; Above 20 mm – highly active

Table 3: Antifungal activity of Ligands and their Ruthenium(II) complexes

| Test Drug                | Zone of Inhibition (mm) |             |             |              |                   |             |             |              |
|--------------------------|-------------------------|-------------|-------------|--------------|-------------------|-------------|-------------|--------------|
|                          | <i>A.niger</i>          |             |             |              | <i>C.albicans</i> |             |             |              |
|                          | 25<br>µg/mL             | 50<br>µg/mL | 75<br>µg/mL | 100<br>µg/mL | 25<br>µg/mL       | 50<br>µg/mL | 75<br>µg/mL | 100<br>µg/mL |
| L1                       | 10                      | 12          | 13          | 15           | 10                | 11          | 13          | 15           |
| L2                       | 12                      | 14          | 16          | 17           | 13                | 16          | 21          | 25           |
| 1                        | 15                      | 18          | 20          | 24           | 12                | 15          | 18          | 22           |
| 2                        | 15                      | 20          | 25          | 28           | 20                | 22          | 26          | 29           |
| Clotrimazole<br>Standard | -                       | -           | -           | 35           | -                 | -           | -           | 20           |

Note: Zone size less than 15 mm – Least active; 16 – 20 mm – moderately active; Above 20 mm – highly active

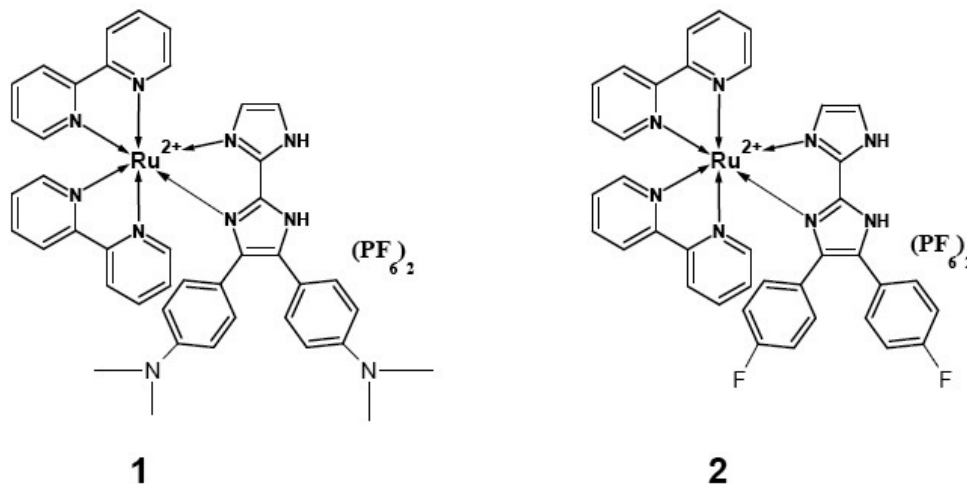


Figure 1: Structure of mononuclear ruthenium(II) complexes

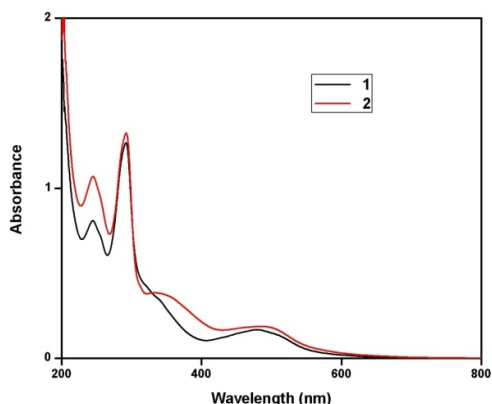
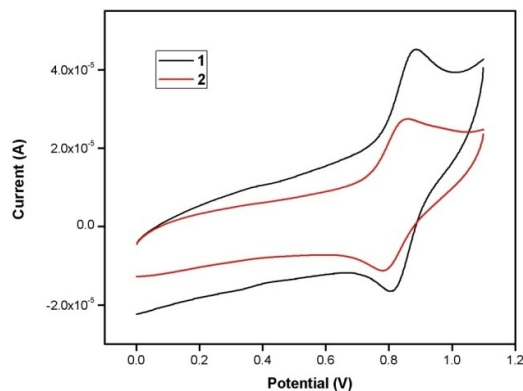


Figure 2: Electronic absorbance spectra of complexes 1 and 2 in acetonitrile.

Figure 3: Cyclic voltammograms of complexes 1 and 2 in acetonitrile against SCE at a scan rate of 100 mVs<sup>-1</sup>

## RESULTS AND DISCUSSION

### Synthesis and Characterization

Ruthenium(II) complexes were synthesized by direct reaction of  $[\text{Ru}(\text{bpy})_2\text{Cl}_2] \cdot 2\text{H}_2\text{O}$  with the appropriate mole ratios of ligands in ethanol-water mixture. Saturated aqueous solution of ammonium hexafluorophosphate was added to precipitate the complexes as hexafluorophosphate salts and characterized by EI-MS, IR, UV and elemental analyses. The positive ion electron ionization mass spectra of the ruthenium(II) complexes

1 and 2 showed a major peak at 1076.71 and 1026.23 respectively. The analytical and mass spectral data are consistent with the proposed formula of the ruthenium(II) complexes. The IR spectra of the free ligands and their ruthenium(II) complexes were compared. In the IR spectrum of both complexes, absorption bands appeared in the region  $1379 - 1462 \text{ cm}^{-1}$  indicates the presence of aromatic skeleton. The IR spectra show the characteristic peaks for the imidazole N-H stretch at  $3429$  and  $3394 \text{ cm}^{-1}$  for the complex 1 and 2 respectively. In the IR spectra of free ligands L1 and L2, the bands due to  $\nu\text{NH}$

absorption appeared at 3479 and 3435  $\text{cm}^{-1}$  respectively. **Figure 2.** depicts the UV-vis spectra of ruthenium(II) complexes recorded in acetonitrile at room temperature. The ground state of ruthenium(II) ( $t_{2g}^6$  configuration) is  $^1A_{1g}$ . For a hexacoordinate ruthenium(II) complex, four transitions corresponding to  $^1A_{1g} \rightarrow ^3T_{1g}$ ,  $^1A_{1g} \rightarrow ^3T_{2g}$ ,  $^1A_{1g} \rightarrow ^1T_{1g}$  and  $^1A_{1g} \rightarrow ^1T_{2g}$  are possible. The electronic spectra of the complexes showed high intensity  $\pi-\pi^*$  transitions in the 279-283 nm range for bipyridine ligand. The peaks observed in the region 321-329 nm were attributed to the ligand molecules **L1** and **L2**. The visible region of both complexes exhibited weak and broad absorption bands which are due to ruthenium(II)  $d-\pi^*$  MLCT in the 474-478 nm range. This data suggests octahedral geometry for both ruthenium(II) complexes.

Electrochemical studies were performed for both in non-aqueous medium, and the relevant electrochemical results are gathered in **Table 1**. Both the complexes show reversible electrochemical wave attributable to Ru(II)/Ru(III) couple. The half-wave potential ( $E_{1/2}$ ) has been found to be +0.8698 V for the complex **1** and +0.8395 V for the complex **2**. During the forward scan **1** shows a quasi-reversible anodic peak at +0.9095 V and cathodic peak at +0.8301 V with the peak separation of 79 mV. On the other hand complex **2** exhibits anodic peak at +0.8770 V and cathodic peak at +0.8019 V with the peak separation of 75 mV. These peaks are due to one electron Ru(II)/Ru(I) redox couple. The typical CV responses of the present complexes are depicted in **Figure 3**. Based on the analytical and spectral data, both the complexes are proposed to have octahedral geometry.

#### Antimicrobial screening

The antimicrobial activities of both the ligands (**L1** and **L2**) and their ruthenium(II) complexes (**1** and **2**) were studied by agar disc diffusion method and the results were shown in **Table 2** and **3**. In vitro antimicrobial activity of a test drug is measured in terms of zone of inhibition produced. Higher the diameter of zone higher is the microbial growth inhibition. It is observed that the growth inhibition activities of the test compounds increase with increase of concentrations of test compounds. A comparison of the activities of the ligands and their complexes against *S.aureus* shows the order: **2** > **1** > **L1** > **L2**. It is to be noted that these compounds exhibit greater activity than the standard Gentamycin.

Comparing the antibacterial activities of test drugs against *B.subtilis* shows the order: **1** > **2** > **L1** > **L2**. In the case of *E.coli* the activities decrease in the order: **1** > **2** > **L2** > **L1**. When the test drugs are assayed against *P.aeruginosa*, it is observed that compound **2** display greater activity and the order of activity shown by other compounds is **2** > **1** > **L1** > **L2**. Thus it is seen that the compounds tested are sensitive to the bacteria used, and all the compounds tested are much more active than the standard antibacterial drug namely gentamycin. The antifungal activity results furnished in **Table 3** indicate that the test drugs show enhanced activity against the test fungi (*A.niger* and *C.albicans*) when the concentrations of drugs are increased. Also the test drugs are less sensitive against the fungi compared to the standard drug viz. clotrimazole. The activities of test drugs against *A.niger* decrease in the order: **2** > **1** > **L2** > **L1**. The sensitivities of test drugs to *C.albicans* are found to decrease in the order: **2** > **L2** > **1** > **L1**. The newly synthesized compounds showed zone of inhibition ranging from 9 to 29 mm. Antimicrobial activity of the newly synthesized ligands and their ruthenium(II) complexes were compared. The results showed that the complexes showed pronounced activity than that of the ligands. This might be explained by Tweedy's chelation therapy<sup>24,25</sup>. The positive charge on the metal ion is partly

reduced by the formation of coordinate bond between the metal ion and the synthesized ligands. This results in increasing the delocalization nature of  $\pi$ -electrons thereby increasing the lipophilic nature of the synthesized complexes.

#### CONCLUSION

Two new ruthenium(II) complexes derived from substituted benzils and imidazole aldehyde have been synthesized successfully.  $[\text{Ru}(\text{bpy})(\text{L1})](\text{PF}_6)_2$  (**1**) and  $[\text{Ru}(\text{bpy})(\text{L2})](\text{PF}_6)_2$  (**2**) were characterized using various spectroscopic and electrochemical techniques. The electrochemical properties of the complexes have been found to be quasi-reversible. From the antimicrobial studies, it has been shown clear that the ruthenium(II) complexes exhibited greater antimicrobial activities compared to that of ligands. The complexes show better antibacterial activity against Gram positive bacteria rather than gram negative bacteria.

#### ACKNOWLEDGEMENT

We wish to thank SAIF-Cochin for carrying out elemental analysis. Also SAIF-IITM is gratefully acknowledged for doing EI mass spectrometry. MK thanks UGC, New Delhi, India, for providing financial support in the form of MRP.

#### REFERENCES

- Li F, Mulyana Y, Feterl M, Warner JM, Collins JG, Keene FR. The antimicrobial activity of inert oligonuclear polypyridylruthenium(II) complexes against pathogenic bacteria, including MRSA. Dalton Transactions 2011; 40:5032-5038.
- Mugge C, Liu R, Gorls H, Gabbiani C, Michelucci E, Rudiger N, et al. Novel platinum(II) compounds with O,S bidentate ligands: synthesis, characterization, antiproliferative properties and biomolecular interactions. Dalton Transactions 2014; 43:3072-3086.
- Gabano E, Ravera M, Osella D. Pros and cons of bifunctional platinum(IV) antitumor prodrugs: two are (not always) better than one. Dalton Transactions 2014; 43:9813-9820.
- Hartinger CG, Dyson PJ. Bioorganometallic chemistry-from teaching paradigms to medicinal applications. Chemical Society Review 2009; 38:391-401.
- Farrer NJ, Salassa L, Sadler PJ. Photoactivated chemotherapy (PACT): the potential of excited-state d-block metals in medicine. Dalton Transactions 2009; 10690-10701.
- Song H, Kaiser JT, Barton JK. Crystal structure of  $\Delta$ - $[\text{Ru}(\text{bpy})_2\text{dppz}]^{2+}$  bound to mismatched DNA reveals side-by-side metalloinsertion and intercalation. Nature Chemistry 2012; 4:615-620.
- Gorman BA, Francis PS, Barnett NW. Tris(2,2'-bipyridyl)ruthenium(II) chemiluminescence. Analyst 2006; 131:616-639.
- Galanski M, Arion VB, Jakupec MA, Keppler BK. Recent developments in the field of tumor-inhibiting metal complexes. Current Pharmaceutical Design 2003; 9:2078-2089.
- Sava G, Gagliardi R, Bergamo A, Alessio E, Mestroni G. Treatment of metastases of solid mouse tumours by NAMI-A: comparison with cisplatin, cyclophosphamide and dacarbazine. Anticancer Research 1979; 19:969-972.
- Li L, Cao W, Zheng W, Fan C, Chen T. Ruthenium complexes containing 2,6-bis(benzimidazolyl)pyridine derivatives induce cancer cell apoptosis by triggering DNA damage-mediated p53 phosphorylation. Dalton Transactions 2012; 41:12766-12772.

11. Wong E, Giandomenico CM. Current status of platinum-based antitumor drugs. *Chemical Review* 1999; 99:2451-2466.
12. Farrell N. *Platinum-based drugs in cancer therapy*. Totowa (NJ): Humana Press; 2000.
13. Wheate NJ, Collins JG. Multi-nuclear platinum complexes as anti-cancer drugs. *Coordination Chemistry Review* 2003; 241:133-145.
14. Anthonysamy A, Balasubramanian S, Shanmugaiah V, Mathivanan N. Synthesis, characterization and electrochemistry of 4'-functionalized 2,2':6',2"-terpyridine ruthenium(II) complexes and their biological activity. *Dalton Transactions* 2008; 28(16):2136-2143.
15. Dwyer FP, Gyarfás EC, Rogers WP, Koch JH. Biological activity of complex ions. *Nature* 1952; 170:90-95.
16. Swapna D, Sivagami B, Manasa K, Rajita G, Alagarsamy V. Synthesis and evaluation of novel thiazolidinedione derivatives for antidiabetic activity. *Int. Res. J. Pharm.* 2016;7(5):15-19 <http://dx.doi.org/10.7897/2230-8407.07544>
17. Bolhuis A, Hand L, Marshall JE, Richards AD, Rodger A, Aldrich-Wright J. Antimicrobial activity of ruthenium-based intercalators. *European Journal of Pharmaceutical Sciences* 2011; 42:313-317.
18. Lam PL, Lu GL, Hon KM, Lee KW, Ho CL, Wang X, et al. Development of ruthenium(II) complexes as topical antibiotics against methicillin resistant *Staphylococcus aureus*. *Dalton Transactions* 2014; 43:3949-3957.
19. Fleming A. On the antibacterial action of cultures of a penicillium, with special reference to their use in the isolation of *B. influenzae*. *British Journal of Experimental Pathology* 1929; 10:11-18.
20. Simmons KJ, Chopra I, Fishwick CW. Structure-based discovery of antibacterial drugs. *Nature Reviews Microbiology* 2010; 8:501-510.
21. Sisko J, Kassick AJ, Mellinger M, Filan JJ, Allen A, Olsen MA. An investigation of imidazole and oxazole syntheses using aryl-substituted tosmic reagents. *Journal of Organic Chemistry* 2000; 65: 1516-1524.
22. Yang X, Chen L, Liu Y. Ruthenium methylimidazole complexes induced apoptosis in lung cancer A549 cells through intrinsic mitochondrial pathway. *Biochimie* 2012; 94:345-353.
23. Bando T, Iida H, Tao ZF, Narita A, Fukuda N, Yamori T, et al. Sequence specificity, reactivity, and antitumor activity of DNA-alkylating pyrrole-imidazole diamides. *Chemical Biology* 2003; 10: 751-758.
24. Tweedy BG. Plant extracts with metal ions as potential antimicrobial agents. *Phytopathology* 1964; 55:8-13.
25. Anjaneyulu Y, Rao RP. Preparation, Characterization and antimicrobial activity studies on some ternary complexes of Cu(II) with acetylacetone and various salicylic acids. *Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry* 1986; 16: 257-272.

**Cite this article as:**

Mathiyalagan Kiruthika, Rajendran Sivasankari, Ramasamy Elayaperumal, Chellamuthu Hariharan, Periasamy Dharmalingam. Antimicrobial activities of Biimidazole based mixed ligand Ruthenium(II) complexes. *Int. Res. J. Pharm.* 2016;7(8):28-32 <http://dx.doi.org/10.7897/2230-8407.07893>

Source of support: UGC, New Delhi, India, Conflict of interest: None Declared

Disclaimer: IRJP is solely owned by Moksha Publishing House - A non-profit publishing house, dedicated to publish quality research, while every effort has been taken to verify the accuracy of the content published in our Journal. IRJP cannot accept any responsibility or liability for the site content and articles published. The views expressed in articles by our contributing authors are not necessarily those of IRJP editor or editorial board members.