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The Chemistry of Elements

Rubidium, Tellurium, Ruthenium and Gadolinium

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Contents

Preface

This book contains eight chapters that detail the chemistry of several elements. Chapter One provides an overview of in vitro antiproliferative and cytotoxic activity of novel Ru (II)-polypyridine complexes on SK-MEL-28 and normal L6 cell lines. Chapter Two discusses the successful development of organometallic complexes as potential anticancer drugs in light of their adaptable structural chemistry and creative modes of action that target nucleic acids and other enzymes. Chapter Three details the design, structural Diversity, and luminescence properties of gadolinium-based solid state phosphors. Chapter Four considers the main homogeneous and heterogeneous catalysts based on ruthenium that are used for the hydrogenation of dienes and compounds with a conjugated diene system. Chapter Five elaborates on the magneto-optical effects of rubidium atoms obtained by applying magnetic and optical fields. Chapter Six presents the biogeochemistry of rubidium. Chapter Seven assesses the ecological state of brown forest acidic soil when contaminated with chemical compounds of tellurium. Finally, Chapter Eight discusses the function of ruthenium complexes in neurological disorders.

Chapter 1

An Evaluation of *In Vitro* Antiproliferative and Cytotoxic Activity of Novel Ruthenium (II)-Polypyridine Complexes on SK-MEL-28 and Normal L6 Cell Lines

Santhiya Sivaraman[1], PhD
Arul Mary Selvaraj[2]
and Sheeba Daniel[1,*], PhD

[1]Department of Chemistry, Holy Cross College (Autonomous), Nagercoil, Tamil Nadu, India
[2]Department of Basic Engineering, Government Polytechnic College, Nagercoil, Tamil Nadu, India

Abstract

Ruthenium complexes have shown great potential and have generated interest in the subject of extensive drug discovery efforts and have acted as novel anticancer drugs by overcoming the limitations of cis-platin. The ligands present in the complexes are capable of undergoing DNA intercalation to cause cell death, a property ideal for applications in photoactivated cancer drug design. The superficial spreading of melanomas that lack melanin pigment can be treated by *in vivo* and in vitro methods. An increasing number of chemo-preventive agents have been shown to stimulate apoptosis in pre-malignant and malignant cells *in vitro* or *in vivo*. This book chapter provides an overview of *in vitro* antiproliferative and cytotoxic activity of novel Ru (II)-polypyridine complexes on SK-MEL-28 and normal L6 cell lines.

[*] Corresponding Author's Email: sheebadaniel@holycrossngl.edu.in.

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The *in vitro* antiproliferative, cytotoxic, and apoptotic activity of six $[Ru(NN)_2L_2]^{2+}$ complexes with intercalating ligands (NN = 2,2′-bipyridine (bpy) and 1,10-phenanthroline (phen); L = 3-benzoyl-picolinic acid (bzpic), 4-Amino-5-(4-pyridyl)-4H-1,2,4 triazole-3-thiol (apytrzSH) and 5-(3-pyridyl)-4H-1,2,4-triazole-3-thiol) (pytrzSH) on SK-MEL-28 and normal L6 cell lines are determined by the direct microscopic, MTT assay and fluorescent microscopic methods. The changes in the morphology of the selected cell lines are determined by direct microscopic methods that are purely based on concentration through dose and time-dependent manner. All the synthesized complexes show a late apoptotic effect on SK-MEL-28 cell line and an early apoptotic effect on the L6 cell line. The obtained results indicate that the antiproliferative and cytotoxic activities of the synthesized complexes depend on the nature of the ligands present in the complexes. Thus, the biological activities of the synthesized complexes provide a promising path for future research in clinical diagnosis as therapeutic agents.

Keywords: ruthenium (II)-polypyridine complexes, antiproliferative activity, cytotoxic activity, apoptotic activity, SK-MEL-28 cell line, normal L6 cell line

Introduction

Cancer is a major health problem and is also known as a silent killer. Cancer originates when the body's normal control mechanism stops working and pays the way for the uncontrolled number of cell divisions and the mutation of normal tissues or cells. These uncontrolled divisions are caused by reactive oxygen species (ROS), where they extremely alter the tissue interstitial containing the protease or antiprotease enzymes and oxidize the normal cells and tissue by the degradation of essential cellular components. ROS are the primary causes of the undesired processes such as ageing, inflammatory and other chronic diseases. They exhibit an important physiological role as free radicals, but they may also engage the toxic effects on the whole human body. The increasing number of cancer incidents lead to increasing demand for cancer treatment.

Transition metal complexes have been studied for cancer treatment as they present different properties, such as different geometries, redox activity, and the ability to bind with different biomolecules, which may interfere with their cytotoxic activity. The platinum-based metallodrugs, which are very efficient in cancer treatment, nevertheless, have resistance and side effects such as

nephrotoxicity, and ototoxicity, among others, severely limit the clinical application of platinum-based treatments. Therefore, the search for new antitumor drug alternatives is one of the most active areas of inorganic medicinal chemistry and has become necessary and urgent.

In the search for novel non-platinum metal-based antitumor agents with a wide range of activity and fewer side effects than those of platinum drugs and their analogs. In recent years, ruthenium-based complexes have received much attention due to their anticancer properties. Over the last few decades, interest in ruthenium polypyridyl complexes as promising in vitro antitumor agents has grown. These molecules have several forms of coordination with metal ions, such as monodentate (S) and bidentate (N, S) or (O, S), in which the latter forms are most described in the literature.

Some ruthenium compounds interact with DNA and have an affinity towards proteins present in the blood, such as transferrin and albumin, which can be interesting due to the ability of these biomolecules to transport drugs in the body. In addition, having different atoms to coordinate with the metal ions, the possibility of altering substituent groups in the molecules enables the synthesis of a considerable number of new molecules with significant structural changes, which make them even more interesting for the coordination chemistry area and has obtained promising results in biological applications.

Ruthenium complexes have certain characteristics that make them attractive as potential chemotherapeutics for different diseases. Ruthenium compounds can easily access three different oxidation states II, III, and possibly IV in biological fluids. Ruthenium (III) compounds could potentially behave as pro-drugs as they can be reduced to ruthenium (II) derivatives in solid tumor masses where the low content of oxygen may act as a reducing environment. As platinum-based drugs, ruthenium compounds can exchange N and O-donor molecules with the added advantage of forming octahedral complexes which interact with DNA). Lastly, ruthenium derivatives probably use transferrin to accumulate into tumors due to the similarities with iron. Of all the ruthenium compounds reported as potential anticancer agents, there are four main groups that have been studied in more detail and display important antitumor and/or antimetastatic activities and low toxicity. The first group corresponds to ruthenium (III) coordination complexes with two compounds currently undergoing clinical trials, NAMI-A (phase I/II), developed by Sava et al., (2002), and the compound KP1019 and its analog containing Na+ KP1339, developed by Keppler et al., (1993) (phase I/II). These Ru complexes exhibit their antiproliferative activity mostly through inhibition of DNA

replication, protein or enzyme activity, and result in cell arrest or apoptosis (Lenis et al., 2022; De Oliveira et al., 2020; Malgorzata et al., 2014; Liang et al., 2022).

Ruthenium (II) Complexes as Therapeutic Agents

The photophysics and photochemistry of transition metal complexes particularly Ru(II) have attracted chemists due to the combination of excellent photophysical and electrochemical properties. Ruthenium complexes possess several favorable properties due to their high coordination number, the additional coordination sites provided to the metal may potentially be used to fine-tune the properties of the complexes and are suited to rationalize anticancer drug design as that of platinum. The ligand exchange kinetics of Ru(II) complexes are similar to that of Pt(II) complexes, which can therefore function as an antineoplastic agent as compared to other coordination compounds. Therefore, it is the first hypothesis to display anticancer effects due to its direct interaction with DNA as observed for platinum complexes (Antonarakis and Emadi 2010).

The combination of these key properties of Ru(II) complexes allows for the design of drug molecules with selective activation and reduced toxicity from currently utilized platinum-based drugs. Ruthenium polypyridine ($[Ru(NN)_3]^{2+}$) complexes having intercalating ligands are well known for their high relevance as drug candidates due to their unique properties such as chemical stability, variable oxidation states, structural diversity, low toxicity, and ability to mimic iron binding in the biological system (Ang et al., 2011).

The properties such as slow rate of ligand exchange, oxidation states, and ability of ruthenium to mimic iron by binding to serum transferrin, transferrin-dependent and transferrin-independent mechanisms of albumin transport make ruthenium compounds suitable for medicinal use (Allardyce and Dyson 2001; Kratz and Messori 1993; Pongratz et al., 2004). Since rapidly dividing cancer cells require iron, this characteristic of ruthenium mimicking iron in biological systems is advantageous for tumor targeted therapy. Lipophilicity and the charge of the ruthenium complexes are also observed to influence their biological effects (Dwyer et al., 1952).

The redox properties of the central ruthenium atom in a complex are dictated by the stability of the oxidation states due to its coordination environment (Baitalik and Adhikary 1997). The redox potential of ruthenium complexes can be modified to improve drug selectivity in tumor tissues due to

the altered metabolism associated with cancer cells resulting in a low oxygen concentration thus promoting a reductive environment (Antonarakis and Emadi 2010). Cancer cells have a lower pH and higher levels of glutathione (GSH) which further create a strongly reducing environment when compared to normal living cells (Schluga et al., 2006).

Ruthenium trichloride ($RuCl_3$) has been used as a precursor for the synthesis of many Ru(II), and Ru(III), complexes. The ruthenium complexes in the +2 oxidation state are usually diamagnetic and reasonably labile; therefore substitution reactions often proceed with retention of configuration, suggesting an associative mechanism. The synthetic protocols of ruthenium, especially with amine and imine ligands, provide many approaches for the synthesis of new metallopharmaceuticals (Holder et al., 2018). The photophysical properties of the low-lying, MLCT excited states of a series of complexes of the type cis-$Ru(bpy)_2L_2$ constitute a quite large family of coordination compounds (Caspar and Meyer 1983). Due to the attractive photophysical properties, much research has been focused on complexes containing ruthenium metal center has shifted to the use of these complexes in biological systems. In the past 15 years, this family has been the object of extensive investigation related to the interesting photochemical, photophysical, and electrochemical properties of most of its members (Barigelletti et al., 1989).

The chelating ligand presents two nitrogen atoms to the metal center in an almost ideal configuration, with only the rotation in the pyridyl-pyridyl bond being restricted upon complex formation. This results in extremely stable species, even with the more labile metal ions. The two excellent primary sigmadative interactions are further enhanced by the opportunities for overlap between the aromatic π-system and the d orbitals of coordinated transition metal ions (Fletcher 2002). The stable complexes with transition metal ions lead to a well-known heterocyclic entity (Marin 2006).

Ruthenium(II) Polypyridine ($[Ru(NN)_3]^{2+}$) Complexes

Over the past decade, $[Ru(NN)_3]^{2+}$ complexes are widely used as photoactive components in many research areas such as photochemical, solar energy conversion, and molecular electronics. The tris-bipyridine-type Ru(II) complexes are the most commonly used because of their favorable properties, which include a long excited state lifetime of up to $\tau = 1$ μs at ambient temperatures (Abrahamsson et al., 2005).

In the early 1970s investigations took place for the quenching of the luminescent triplet charge-transfer excited state of $[Ru(bpy)_3]^{2+}$ complex by energy transfer. The self-exchange energy transfer processes involve in the designing of $[Ru(NN)_3]^{2+}$ complexes having specific properties are much more difficult to tackle than that of self-exchange electron transfer. Hence, noticed that $[Ru(L)_3]^{2+}$, $[Ru(bpy)(L)_2]^{2+}$ and $[Ru(bpy)_2(L)]^{2+}$ complexes have very different luminescence lifetimes, but practically the same excited state energy (Balzani and Juris 2001). Molecular architectures based on the assembly of metallic cores and aromatic ligands are currently studied compounds in coordination chemistry. The unique combination of chemical stability, excited state reactivity and redox properties are responsible for specific electron and energy transfer processes (Pourtois et al., 2004).

The synthesis of $[Ru(NN)_3]^{2+}$ complexes has become a major area of research for their appealing properties. These properties are tuned by varying the nature and the number of the polypyridine ligands around the Ru(II) metal center, which absorb visible light and emit long wavelength light within the red and near-infrared spectral regions. The long-lived triplet excited states of $[Ru(NN)_3]^{2+}$ complexes show reversible redox properties, and make the complexes highly desirable across numerous research fields (Sun et al., 2015). The octahedral geometry of these complexes pays chemists to readily gain access to molecules with complicated 3-dimensional architectures. Therefore, examining the diverse range of molecular structures that $[Ru(NN)_3]^{2+}$ complexes have been incorporated into the development of new classes of diagnostic and therapeutic agents (Poynton et al., 2017).

Biological Importance of $[Ru(NN)_3]^{2+}$ Complexes

Ruthenium(II) complexes act as potential cellular imaging for antitumor drugs, cellular targeting, and therapeutic agents. These complexes non-covalently interact with biomolecules and lend themselves to design new therapeutic agents. Upon light activation, $[Ru(NN)_3]^{2+}$ complexes may elicit their biological activity. The size of the polypyridine ligand coordinated to the Ru(II) center incorporates more extended aromatic ligands and tends to be of considerable importance and show greater biological activity. The overall function of the Ru(II) complexes is determined by the structural nature of the polypyridine units in the metal complex which mainly focuses on using planar bi- or tri-dentate ancillary ligands (Poynton et al., 2017; Ravi et al., 2019). Complexes derived from these planar heteroaromatic ligands are capable of

covalently binding to DNA once vacant coordination sites are opened through ligand release (Singh and Turro 2004). The aim of discovering anticancer therapeutics is to arrest the proliferation of cancer cells and to elicit cell death by damaging cells. Thus, Ru complexes have shown great potential and generating interest in the subject of extensive drug discovery efforts and act as novel anticancer drugs by overcoming limitations (Incesu et al., 2013; Xu et al., 2014). In addition, related ligands are capable of undergoing DNA intercalation to cause cell death, such properties are ideal for applications in photoactivated cancer drug design. $[Ru(NN)_3]^{2+}$ complexes that have ancillary ligands with denticities of four or above are still underdeveloped. Such ligands introduce geometrical constraints to metal centers, which in turn stabilizes the coordination sphere of the complexes. Since higher denticity, ancillary ligands can result in Ru(II) complexes with different photophysical and photochemical properties than lower denticity ones. In general, the thermally stable $[Ru(NN)_3]^{2+}$ complexes in aqueous solutions are able to absorb in the visible region.

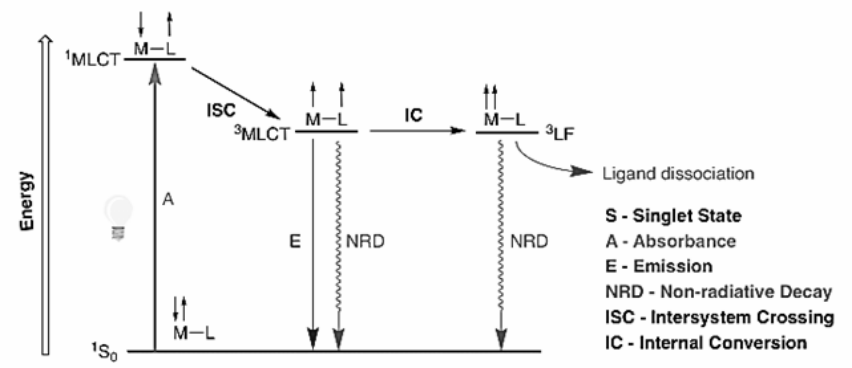


Figure 1. Jablonski diagram for $[Ru(NN)_3]^{2+}$ complex.

The attractive property of Ru(II) complexes towards the application of drug delivery is to accumulate in tumor cells. In addition, most of the $[Ru(NN)_3]^{2+}$ complexes occupy low lying ^{3}MLCT (metal to ligand charge transfer) states with thermally accessible low lying ligand field (^{3}LF) states. It is generally accepted that ligands coordinated to the metal center can be easily dissociated upon irradiation with light at room temperature through the population of the ^{3}LF states. In complexes with low-lying ^{3}MLCT and ^{3}LF states, such as in $[Ru(NN)_3]^{2+}$ complexes, it is generally accepted that those with ^{3}LF states occupying lower energy levels should exhibit greater quantum

efficacy of ligand photodissociation (Figure 1). The energy levels of ^{3}MLCT and ^{3}LF states may not be equal (Li 2018).

DNA provides the "master genetic blueprint" for the construction of each protein required by individual cells through the RNA-mediated processes of transcription and translation. The ability to bind and cleave DNA by interfering with the essential cellular processes of transcription and translation can also be developed as potential therapeutics. Metal complexes also offer distinctive chemical activities, and a variety of binding modes that coordinate directly to DNA Lewis base sites and undergo redox reactions with DNA or generate reactive oxygen-containing species. Ruthenium(II) complexes have been widely used in DNA binding studies because of the sensitivity of their photophysical properties such as luminescence enhancement and absorption hypochromic in the intense MLCT bands. Ruthenium complexes can form covalent bonds to the phosphodiester backbone, sugar residues, or bases of the DNA molecule.

The induction of DNA damage by a drug molecule forms the basis of classical chemotherapy. As a result of genetic instability caused by this binding, cancer cells are unable to affect the correct cell cycle checkpoint responses to induced damage and consequently undergo cell cycle arrest, ultimately leading to apoptosis or programmed cell death (PCD). Rapidly dividing cancer cells are preferentially targeted by a therapeutic regime. Ligand easily interchanged or modified, provides a mechanism to control hydrophobicity, binding affinity, and selectivity in addition to cellular uptake. Judicious selection of ligands and the metal center also allows for tuning the photophysical properties of the complex (Kannan 2016).

Melanoma - Skin Cancer

Skin is the largest organ present in the body which serves as a physical and chemical barrier and protects the body against various harmful environmental agents such as pathogens, UV radiation, and chemicals. UV radiation causes excessive damage to cellular DNA leading to skin cancer. Temperature fluctuation stresses accumulated in the body result in skin carcinogenesis (Iqbal et al., 2019). The rare form of skin cancer is melanoma which is mostly unresponsive to conventional treatments. The early-stage melanoma is cured by surgery whereas late-stage melanoma may be treated with radiation, immunotherapy, and chemotherapy (Ndhundhuma and Abrahamse 2017).

Melanoma is responsible for 75% of all skin cancer-related deaths even though it accounts for less than 5% of all skin cancer cases (Singh et al., 2014). Early detection of primary melanoma is associated with improved survival. The changes in the skin such as soreness, unusual growth, or a change in an existing mole, skin appearance and new growth could turn out to be basal cell and squamous cell carcinoma. Melanocytes are responsible for the production of the dark pigment melanin which is normally present in the skin (Figure 2) (Das et al., 2016). The superficial spreading of melanomas that lack melanin pigment can be treated by in vivo and in vitro methods with an attractive therapeutic target; chemotherapy agents make an important contribution to melanoma in the future (Perera et al., 2014).

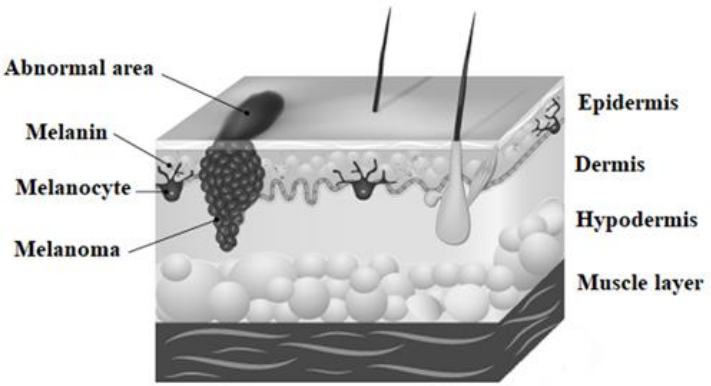


Figure 2. Schematic representation of melanoma.

Melanoma is a malignancy of the melanocyte and a specialized cell-derived embryologically from the neutral crest that contains a unique set of organelles (melanosomes) responsible for the synthesis of melanin (Enochs et al., 1989). Melanoma is a heterogeneous disease that suggests a rich complex aetiology (Marconi et al., 2018). Malignant melanoma is a highly invasive skin cancer arising from the abnormal proliferation of epidermal melanocytes (Matsushita et al., 2010). It is formed by the dysfunction of a single melanocyte. The melanocytes, located at the base of the epidermis are responsible for producing the melanin pigment and can be found in our hair, eyes, and skin (Naves et al., 2017).

Apoptosis is a self-destruction complex and a biochemical process of cells in a multicellular organism. It is a PCD that maintains tissue homeostasis, fetal development, and aging (Popgeorgiev et al., 2018). During apoptosis, the

surrounding cells and cellular macromolecules are digested into smaller fragments. In a controlled fashion the cells are collapsed into smaller intact fragments and are removed by phagocytosis without damage (Fridman et al., 2007). Apoptosis and necrosis are two major mechanisms of cell death. Cells that are damaged by external injury undergo necrosis, while cells that are induced to commit programmed suicide because of internal or external stimuli undergo apoptosis. An increasing number of chemo-preventive agents have been shown to stimulate apoptosis in pre-malignant and malignant cells *in vitro* or *in vivo* (Hussain et al., 2018).

Ruthenium(II)-Polypyridine Complexes and Their Anticancer Activity

Metal complexes exhibit various oxidation states and engage with several negatively charged molecules and thus play a crucial role in drug remedies (Sridevi et al., 2019). Metallodrugs continue as an anticancer agent in the areas of pharmaceutical research paving a new way for researchers to go for new metal-based chemotherapeutical complexes (Singh and Singh 2012). $[Ru(NN)_3]^{2+}$ complexes with several favorable properties are suited to rationalize anticancer drug design as that of platinum (Balakrishnan et al., 2014). $[Ru(NN)_3]^{2+}$ complexes distinct from those of platinum complexes show antitumor activity and exhibit greater efficacy against cancer metastasis than primary tumors. Researchers synthesized numerous ruthenium containing agents and tested for potential anticancer activity (Gligorijevic et al., 2012).

Ruthenium and its complexes are easily absorbed by tumor tissues and are excreted in vivo quickly, in addition, they possess low toxicity and have good anticancer application prospects. Compared with small molecule drugs, ruthenium complexes can provide a unique modular system. The ruthenium metal atom acts as a structural center to support a rigid three-dimensional scaffold of ligands, which could lead to many ruthenium complexes with different structural properties *via* facile ligand substitution or modification with specific receptors of cancer cells or other anti-cancer drugs. Using these methods, not only new complexes with significant anticancer activities can be obtained, but also some predesigned physicochemical properties such as water solubility, lipid solubility, and targeting properties can be precisely achieved. Ru(II) complexes are potential chemotherapeutic drugs that can bind to

various nucleic acid sequences in different modes, such as insertion and groove cross-binding. Thus, the complexes can be used as specific inhibitors for telomerase, DNA topoisomerase, protein kinase, and so on, to regulate cell pathways and induce tumor cell apoptosis (Yang et al., 2018). $[Ru(NN)_3]^{2+}$ complexes as cellular targeting agents lie in the fact that the structural nature of the polypyridyl units dictates the overall function of the metal complex including their solubility, lipophilicity, charge, and their photophysical properties (Ravi et al., 2019).

The introduction of aromatic N-containing ligands such as derivatives of pyridine, imidazole, and phenanthroline to antitumor agents is drawing attention. Many platinum and non-platinum metal complexes with these aromatic N-containing ligands have shown promising *in vitro* and *in vivo* antitumor properties in cisplatin-resistant model systems or against cisplatin-insensitive cell lines (Kostova 2006).

Over the years, sulphur containing compounds have been identified as promising protective agents against different types of cancer. Sulphur compounds are reported as radical scavengers to protect cells from free radicals. It reacts easily with ROS due to its strong nucleophilic property to donate electrons. Recently, sulphur compounds having sulphydryl functional groups (-SH) show a protective effect against cancer by the oxidation of the -SH group. The thiyl radical fragment is very important for radical scavenging and anti-proliferative effects. The 1,3,4-thiadiazole moiety containing-compounds exhibit potential anticancer, antitubercular, and antiulcer properties. The aromaticity of 1,3,4-thiadiazoles is attributed to their potential anticancer agent, enhanced radical scavenging ability and antiproliferative activity.

The DPPH (2,2,diphenyl-picrylhydrazyl) and MTT (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyltetrazolium bromide) assays methods are carried out to evaluate the structural variations of the synthesized compounds for their radical scavenging and cytotoxicity effects against various cell lines. The MTT assay is a sensitive, quantitative, and reliable colorimetric assay that measures the viability, proliferation, and activation of cells (Senthilraja and Kathiresan 2015).

Similar to cisplatin, Ru(III) complexes of 1,2,4-triazoles act as a promising potential drug in anticancer treatment further treated as alternatives to the approved platinum-based anticancer drugs. The commercially available drugs of 1,2,4-triazoles such as rizatriptan which are agents for the acute treatment of migraine headaches still considered as a topic of intensive research (Holm and Straub 2011).

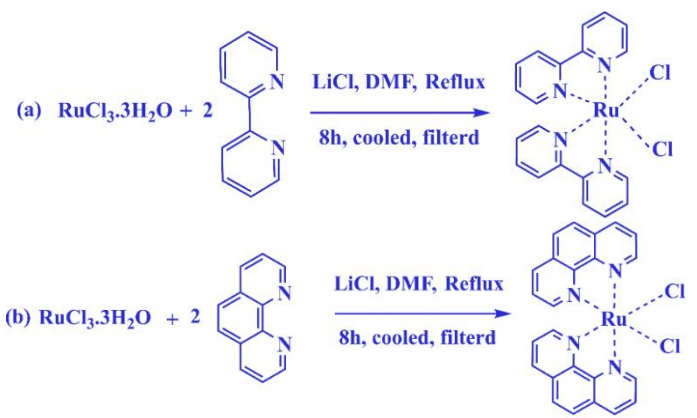
Synthesis of $[Ru(NN)_2L_2]^{2+}$Complexes

The six $[Ru(NN)_2L_2]^{2+}$ complexes {NN = 2,2′-bipyridine (bpy) or 1,10-phenanthroline (phen), L_1 = 3-benzoyl picolinic acid (bzpic), L_2 = 4-amino-5-(4-pyridyl)-4H-1,2,4-triazole-3-thiol (apytrzSH) and L_3 = 5-(3-pyridyl)-4H-1,2,4-triazole-3-thiol (pytrzSH)} taken in the present investigation are mentioned as follows:

1. $[Ru(bpy)_2(bzpic)_2](PF_6)_2$ (Complex A)
2. $[Ru(bpy)_2(apytrzSH)_2](PF_6)_2$ (Complex B)
3. $[Ru(bpy)_2(pytrzSH)_2](PF_6)_2$ (Complex C)
4. $[Ru(phen)_2(bzpic)_2](PF_6)_2$ (Complex D)
5. $[Ru(phen)_2(apytrzSH)_2](PF_6)_2$ (Complex E)
6. $[Ru(phen)_2(pytrzSH)_2](PF_6)_2$ (Complex F)

Synthesis of Precursor Complexes $[Ru(NN)_2Cl_2]$

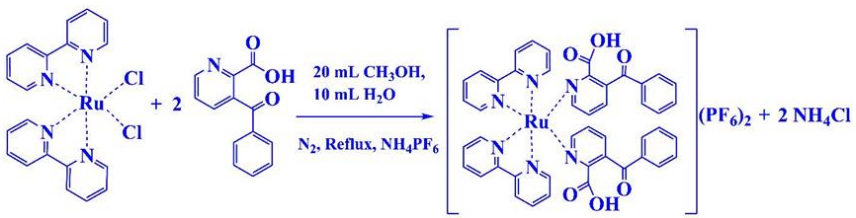
$RuCl_3.3H_2O$, bpy or phen and LiCl are refluxed in DMF for 8 h in the presence of a nitrogen atmosphere. The reaction mixture is cooled to room temperature and filtered the obtained black crystalline substance. The precipitate is washed with double distilled water followed by diethyl ether and dried (Scheme 1). The obtained precursor complexes $[Ru(NN)_2Cl_2]$ are recrystallized from ethanol and used as such for the synthesis of $[Ru(NN)_2(L)_2]^{2+}$ complexes.



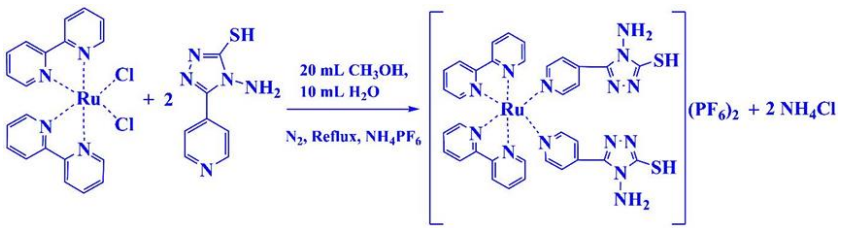
Scheme 1. Synthesis of precursors (a) $[Ru(bpy)_2Cl_2]$ and (b) $[Ru(phen)_2Cl_2]$.

Synthesis of $[Ru(bpy)_2L_2](PF_6)_2$ Complexes

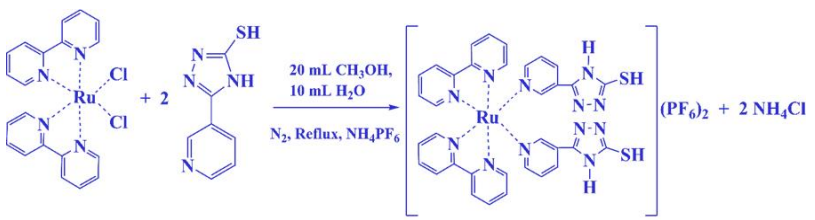
The three $[Ru(bpy)_2L_2](PF_6)_2$ complexes A-C are syntheised separately by refluxing the precursor complex $[Ru(bpy)_2Cl_2]$ with the corresponding ligands $L_1/L_2/L_3$ in 20 mL of methanol for 4 h under nitrogen atmosphere. The solution is allowed to cool at room temperature and filtered to remove any insoluble impurities. A saturated solution of NH_4PF_6 is added dropwise into the corresponding filtrate until a brownish-red precipitate is formed. The product is filtered, washed with cold water and diethyl ether, and further dried in a vacuum desiccator. The synthesized complexes A-C are purified separately by column chromatography using a mixture of methanol and dichloromethane (Schemes 2-4). The purified complexes are collected and stored in a vacuum desiccator for further studies.



Scheme 2. Synthesis of $[Ru(bpy)_2(bzpic)_2](PF_6)_2$ (Complex A).



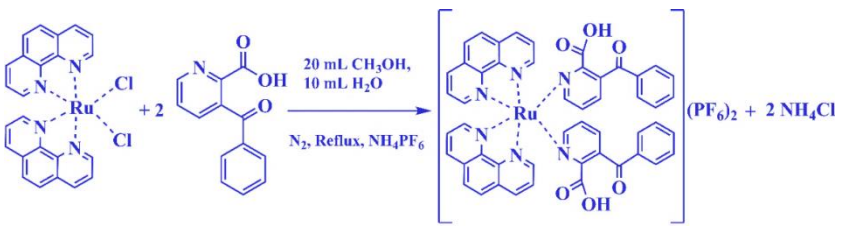
Scheme 3. Synthesis of $[Ru(bpy)_2(apytrzSH)_2](PF_6)_2$ (Complex B).



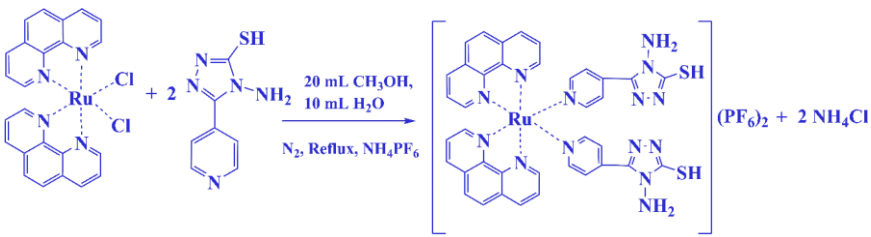
Scheme 4. Synthesis of $[Ru(bpy)_2(pytrzSH)_2](PF_6)_2$ (Complex C).

Synthesis of $[Ru(phen)_2L_2](PF_6)_2$ Complexes

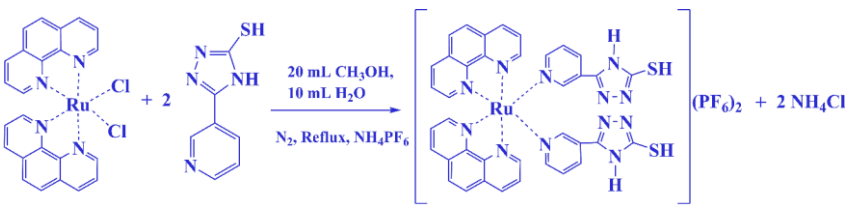
The three $[Ru(phen)_2L_2](PF_6)_2$ complexes D-F are syntheised by refluxing the precursor complex $[Ru(phen)_2Cl_2]$ with the corresponding ligands L_1, L_2 and L_3 in 20 mL of methanol for 4 h under nitrogen atmosphere. The solution is allowed to cool at room temperature and filtered to remove any insoluble impurities. A saturated solution of NH_4PF_6 is added dropwise into the corresponding filtrate until a brownish-red precipitate is formed. The product is filtered, washed with cold water and diethyl ether, and further dried in a vacuum desiccator. The synthesized complexes D-F are purified separately by column chromatography using a mixture of methanol and dichloromethane (Schemes 5-7). The purified complexes are collected and stored in a vacuum desiccator for further studies.



Scheme 5. Synthesis of $[Ru(phen)_2(bzpic)_2](PF_6)_2$ (Complex D).



Scheme 6. Synthesis of $[Ru(phen)_2(apytrzSH)_2](PF_6)_2$ (Complex E).



Scheme 7. Synthesis of $[Ru(phen)_2(pytrzSH)_2](PF_6)_2$ (Complex F).

Characterization of $[Ru(NN)_2L_2]^{2+}$Complexes

The structural investigation of the complexes A-F is performed by elemental analysis, UV, emission, FT-IR, ^{1}H NMR, ^{13}C NMR, and MALDI-TOF mass spectral techniques. The percentage composition of C, H, O, N, and S present in the complexes A-F is determined by elemental analysis. The proposed molecular formula obtained from the elemental analysis for complexes A-F is tabulated in Table 1.

Table 1. Elemental analysis of complexes A-F

Complex	Molecular Formula	Percentage Composition				
		C	H	N	O	S
A	$C_{46}H_{34}N_6O_6Ru.2PF_6$	63.66	3.95	9.68	11.06	-
B	$C_{34}H_{30}N_{14}S_2Ru.2PF_6$	51.58	4.08	24.06	-	7.87
C	$C_{34}H_{28}N_{12}S_2Ru.2PF_6$	57.79	6.57	17.97	-	6.86
D	$C_{50}H_{34}N_6O_6Ru.2PF_6$	66.16	4.06	8.90	10.71	-
E	$C_{38}H_{30}N_{14}S_2Ru.2PF_6$	54.28	3.85	22.72	-	7.43
F	$C_{38}H_{28}N_{12}S_2Ru.2PF_6$	60.16	6.46	16.4	-	6.42

Absorption Spectral Analysis of $[Ru(NN)_2L_2]^{2+}$ Complexes

The charge transfer bands that arise from the changes in the electronic distribution between the metal and the ligands are determined by UV-Visible spectral studies. $[Ru(NN)_3]^{2+}$ complexes absorb UV light and undergo MLCT transition by promoting an electron from the t_{2g} orbitals of the metal (HOMO) having more ruthenium character to the π^* orbitals of the ligand (LUMO) having more pyridine character (Tan et al., 2018). The weak absorption at 360 - 370 nm corresponds to metal centred (MC) transition and the absorption in the region 435 - 550 nm is assigned due to $d\pi$ (Ru)→L MLCT transition thereby assigning a +2 oxidation state to ruthenium possessing an octahedral geometry. The four transitions possible for a hexacoordinate Ru(II) complex correspond to $^1A_{1g}\rightarrow {}^3T_{1g}$; $^1A_{1g}\rightarrow {}^3T_{2g}$; $^1A_{1g}\rightarrow {}^1T_{1g}$ and $^1A_{1g}\rightarrow {}^1T_{2g}$ (Ashok et al., 2007). The MLCT absorption bands are broad at room temperature with evidence for vibronic structure (Thompson et al., 2013). Similar observations are obtained for the absorption spectra of all the complexes A-F which result in an octahedral geometry for the complexes. The absorption spectra of the ligands L_1-L_3 exhibits high energy bands in the UV region assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions. The absorption spectrum of ligand apytrzSH (L_2) is shown in Figure 3.

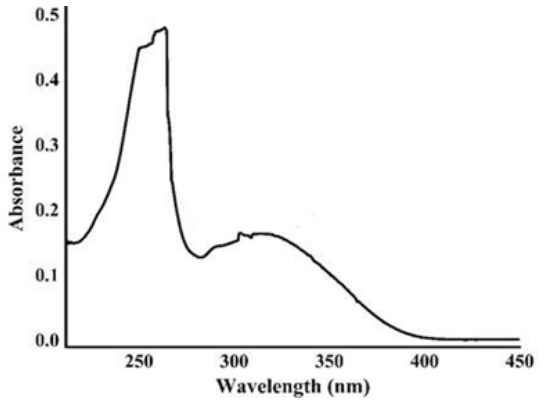


Figure 3. Absorption spectrum of apytrzSH ligand.

The absorption spectra of complexes A-F display two spin allowed π–π* transitions at 220 - 250 and 265 - 292 nm range and these intense absorption bands are due to the presence of ligands present in the complexes. The weak absorption at 340 - 366 nm corresponds to MC transition and the absorption in the region 438 - 478 nm is assigned due to dπ (Ru)→L MLCT transition (Figures 4 and 5). The λ_{max} values of the complexes A-F in aqueous acetonitrile are tabulated in Table 2. The spectral data clearly explains that all the complexes A-F show a hypsochromic shift in the lowest energy MLCT maximum with respect to the MLCT maximum of the Ru(bpy/phen)$_2$Cl$_2$ precursors.

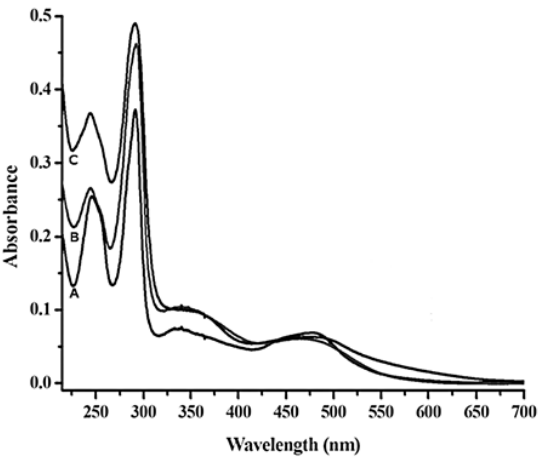


Figure 4. Absorption spectra of $[Ru(bpy)_2(L)_2]^{2+}$ complexes A-C.

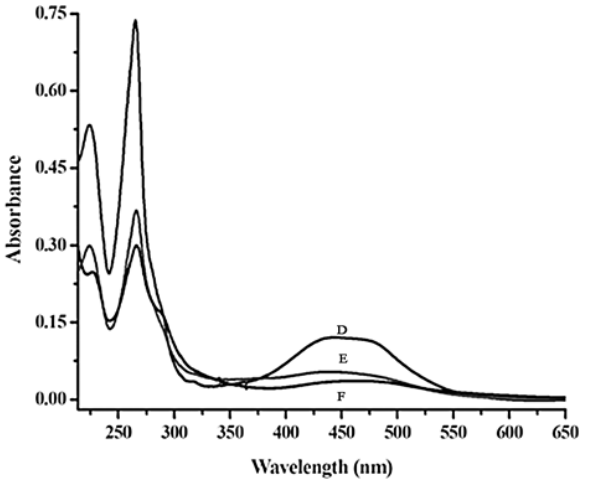


Figure 5. Absorption spectra of $[Ru(phen)_2(L)_2]^{2+}$ complexes D-F.

Table 2. Absorption spectral data of complexes A-F

Complex	**Absorption Maximum (λ_{max}), nm**
$[Ru(bpy)_2Cl_2]$	296.5, 372, 541
A	246, 291.5, 340, 478
B	244.5, 292.5, 340, 464
C	245, 291, 365.5, 476
$[Ru(phen)_2Cl_2]$	266.5, 353.5, 530
D	224, 265, 361.5, 445
E	224, 265.5, 363.5, 438.5
F	227.5, 266, 365.5, 464

The replacement of two chloride ligands by the ligands ($L_1/L_2/L_3$) containing pyridine rings shift the MLCT absorption to a shorter wavelength region. A small red shift is observed in the MC peak of the complexes D, E, and F containing highly conjugated phen ligands which broadens the absorption band when compared to the $[Ru(phen)_2Cl_2]$ precursor (Tan et al., 2013). This change in the absorbance value is also due to the size of the PF_6^- counter ions (Patil-Deshmukh et al., 2020).

Emission and Lifetime Analysis of $[Ru(NN)_2L_2]^{2+}$ Complexes

The emission and fluorescent lifetime spectral properties of the complexes A-F are carried out in acetonitrile under a nitrogen atmosphere at room

temperature (Table 3). The complexes A, B and C from the precursor $[Ru(bpy)_2Cl_2]$ by replacing the chloride ligands with L_1 - L_3 show emission at 590 - 665 nm, whereas the complexes D, E, and F from the precursor $[Ru(phen)_2Cl_2]$ show emission at 580 - 635 nm respectively. The complexes show emission with slight intensity originating from dπ (Ru)→L MLCT transition which is mainly attributed to the non-radiative decay process and it is more effective in bpy complexes A-C as compared to phen complexes D-F (Mohite et al., 2019). The emission energy of all complexes is sensitive to the bigger size of the PF_6^- counter anion when compared to other counter ions such as NO_3^-, BF_4^-, and ClO_4^- (Campagna et al., 2007).

Table 3. Emission and Lifetime data of complexes A-F

Complex	Emission Maximum (λ_{max}), nm	Lifetime (τ), ns
A	649 and 663	0.558
B	645	2.891
C	591	3.563
D	620	33.29
E	633	0.186
F	584	2.608

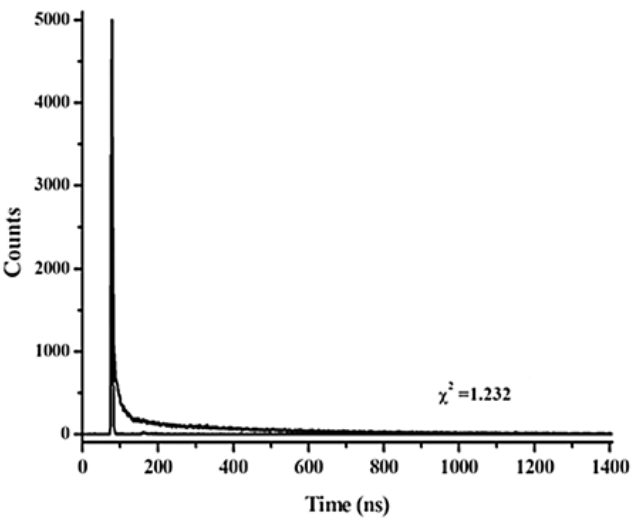


Figure 6. Lifetime analysis of complex D