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FROM MOLECULAR LIGHT TO BIOLOGICAL ACTION: EMERGING APPLICATIONS OF RUTHENIUM(II) POLYPYRIDYL COMPLEXES

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Abstract
Ruthenium(II) polypyridyl complexes have developed into a versatile family of coordination compounds at the intersection of inorganic chemistry, photochemistry, medicinal chemistry and molecular biology. Their significance arises from the ability of the ruthenium centre and coordinated polypyridyl ligands to provide a combination of structural stability, tunable electronic pro perties, metal-to-ligand charge-transfer transitions, luminescence and redox activity. These characteristics enable the complexes to recognize biomolecular targets and respond to external stimuli such as visible light. In particular, the extended aromatic surfaces of ligands such as 1,10-phenanthroline and dipyridophenazine can facilitate interactions with DNA through intercalation, groove association and electrostatic attraction. Such interactions have stimulated investigations into their use as molecular probes , cellular imaging agents and anticancer compounds. Light-responsive Ru(II) complexes have further expanded the scope of this chemistry through photodynamic therapy and photoactivated chemotherapy, in which irradiation can generate reactive species or activate otherwise less reactive molecular structures. Beyond therapeutic applications, ruthenium polypyridyl systems have been explored for antimicrobial phototherapy, chemical sensing, photocatalysis, solar-energy conversion and molecular devices. Recent studies increasingly emphasize long-wavelength absorption, organelle targeting, multimodal imaging and oxygen-independent photochemical mechanisms. This review presents an integrated discussion of molecular design, photophysical characteristics, DNA recognition, biological applications and photocatalytic potential of Ru(II) polypyridyl complexes, with particular attention to structure–property relationships and future challenges.

Keywords: Ruthenium(II); polypyridyl complexes; DNA recognition; photodynamic therapy; photo activated chemotherapy; anticancer activity; molecular imaging; photocatalysis; biosensing

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1. Introduction

Transition-metal complexes with controllable chemical and biological functions are important across inorganic chemistry, materials science and medicinal chemistry. Ruthenium is particularly attractive because of its accessible oxidation states, versatile coordination chemistry and favourable kinetic and photophysical properties. Ru(II) polypyridyl complexes have therefore become important platforms for molecular design and functional applications [1,2].

The fundamental chemistry of these complexes is associated with ligands such as 2,2′-bipyridine, 1,10-phenanthroline, terpyridine and extended π-conjugated ligands. Their coordination gives rise to characteristic metal-to-ligand charge-transfer (MLCT) transitions and long-lived excited states, which underpin their optical and redox behaviour [1,3]. The field has subsequently expanded from DNA recognition to cellular imaging, therapeutics and theranostics [2].

An important contemporary direction is to understand biological activity beyond simple DNA binding. Cellular uptake, subcellular localization, protein interactions, DNA damage, reactive oxygen species and photochemical processes can all contribute to biological responses. Recent work has specifically examined the relationship between Ru(II) polypyridyl complexes and DNA-damage response pathways [4].

2. Molecular Design and Photophysical Characteristics

Table 1. Representative Ru(II) polypyridyl complexes and characteristic features

Complex / ligand system	Structural feature	Major property	Representative application
$[Ru(bpy)_3]^{2+}$	Three bipyridine ligands	MLCT photochemistry	Photoredox chemistry; energy transfer [1,3]
$[Ru(phen)_3]^{2+}$	Three phenanthroline ligands	Luminescence; DNA association	DNA recognition; sensing [1,2]
$[Ru(bpy)_2(dppz)]^{2+}$	Extended dppz π-system	DNA-dependent luminescence	DNA imaging; molecular sensing [1,5]
Ru(II)–terpyridine systems	Tridentate ligand framework	Tunable electronic properties	Sensing; photochemistry [2]
Ru(II) mixed-ligand complexes	Different functional ligands	Multifunctionality	Imaging; therapy [2,7]
Dinuclear Ru(II) systems	Two ruthenium centres	Enhanced energy/electron transfer	Photocatalysis; biological applications [12]

Sources: Numbered references correspond to the reference list in the review manuscript.

Ru(II) polypyridyl complexes commonly possess an octahedral coordination environment. Chelating N-donor ligands provide structural stability while permitting systematic modification of charge, conjugation, steric environment, solubility and lipophilicity. The archetypal $[Ru(bpy)_3]^{2+}$ system illustrates how ligand-centered π* orbitals can participate in MLCT excitation [1,3].

Extended aromatic ligands can substantially alter both photophysical and biological behaviour. Dipyridophenazine (dppz), for example, has an extended π-system that supports DNA association and environment-sensitive luminescence. Ru–dppz complexes have consequently become useful platforms for DNA recognition, imaging and sensing [5].

Photophysical properties can be adjusted through ligand conjugation, electronic substituents, rigidity, molecular charge, number of metal centres and hydrophilic/lipophilic balance. These parameters influence absorption, emission, excited-state lifetime, redox potentials and reactive oxygen species generation [2,5].

3. DNA Recognition by Ru(II) Polypyridyl Complexes

Table 2. Major interaction modes of Ru(II) polypyridyl complexes with DNA

Interaction mode	Structural requirement	Principal interaction	Possible consequence
Electrostatic association	Cationic Ru(II) complex	Phosphate backbone	Initial DNA association [1,5]
Groove binding	Appropriate molecular shape	Hydrogen bonding / van der Waals interactions	Sequence or shape recognition [1,5]
Intercalation	Planar aromatic ligand	Insertion between base pairs	DNA structural perturbation [1,5]
Partial intercalation	Extended but non-planar ligand	Base-pair and groove contacts	Strong molecular recognition [1,5]
Photochemical interaction	Photoactive Ru(II) centre	ROS / electron transfer	DNA damage [4,8]
Covalent interaction	Suitable ligand-exchange properties	Nucleobase coordination	Chemical modification of DNA [2,6]

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DNA remains a major molecular target of Ru(II) polypyridyl complexes. Several interaction modes are possible, including electrostatic association, groove binding and intercalation [1,5]. The cationic character of many complexes promotes association with the negatively charged phosphate backbone, whereas planar aromatic ligands can insert between base pairs.

The Ru–dppz family is particularly important because DNA binding can substantially alter its luminescence, providing the basis of the well-known molecular "light-switch" behaviour [5]. Structural changes in the polypyridyl ligand can therefore be used to regulate both recognition and optical response.

Current research increasingly connects molecular DNA interaction with cellular DNA-damage response. The nature of the lesion, its recognition by repair pathways and the resulting cell fate are important for understanding the therapeutic potential of these complexes [4].

4. Anticancer Potential

Table 3. Biomedical applications of Ru(II) polypyridyl complexes

Application	Main molecular event	Potential outcome
DNA recognition	Intercalation / groove association	Molecular targeting [1,5]
Cancer therapy	DNA damage; ROS; mitochondrial effects	Apoptosis or growth inhibition [2,6,7]

Photodynamic therapy	Light-induced reactive species	Photoactivated cell killing [8,9]
Photoactivated chemotherapy	Light-induced ligand release or activation	Spatially controlled therapy [2,8]
Cellular imaging	Ru(II) luminescence	Visualization of cells / organelles [2,7,11]
Molecular sensing	Environment-dependent emission	Detection of biomolecules [1,5,11]
Antimicrobial PDT	Photoinduced ROS	Microbial inactivation [10]

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The limitations of conventional platinum chemotherapy have stimulated the development of alternative metal-based anticancer agents. Ru(II) polypyridyl complexes are attractive because the same molecular framework can provide recognition, imaging and therapeutic functions [2,6].

Reported mechanisms include DNA damage, mitochondrial dysfunction, oxidative stress, enzyme inhibition, organelle accumulation and apoptosis. The biological response is strongly structure-dependent; modifications that change lipophilicity, charge or ligand planarity can alter cellular uptake and localization [2,6].

A notable development is the design of complexes that combine anticancer activity with cellular imaging. Such systems illustrate the movement from single-function cytotoxic compounds toward multifunctional and theranostic ruthenium platforms [2,7].

5. Photodynamic Therapy and Photoactivated Chemotherapy

Photodynamic therapy (PDT) uses a photosensitizer that, after light absorption, produces reactive species capable of damaging biological targets. Ru(II) polypyridyl complexes are suitable photosensitizers because their excited states can participate in energy- and electron-transfer processes [8]. Both Type I radical pathways and Type II singlet-oxygen pathways may contribute, depending on molecular structure and biological environment.

A major design challenge is the wavelength of activation. Long-wavelength and near-infrared approaches are attractive because they can improve light penetration. Two-photon excitation has consequently emerged as an important strategy for both imaging and phototherapy [9]. Antibacterial PDT is another growing application, with Ru(II) complexes being investigated as light-activated antimicrobial agents [10].

Photoactivated chemotherapy provides a related but mechanistically distinct strategy in which irradiation triggers a chemical transformation that generates a more active species. This concept offers temporal and spatial control and complements conventional chemotherapy [2,8].

6. Cellular Imaging and Molecular Sensing

The luminescence of Ru(II) polypyridyl complexes provides useful characteristics for cellular imaging, including relatively long excited-state lifetimes, photostability and environmental sensitivity [2,11]. Ligand modification can promote localization in the nucleus, mitochondria, lysosomes or other cellular compartments.

Conjugation with peptides, targeting groups or nanomaterials can further modify uptake and biodistribution. These approaches have enabled the development of probes for cellular imaging, biomolecular recognition and multimodal theranostics [2]. The ability of Ru–dppz complexes to change luminescence upon DNA interaction is an especially useful example of molecular sensing [5].

7. Antimicrobial Applications

Antimicrobial resistance has stimulated interest in alternative mechanisms of microbial control. Ru(II) polypyridyl complexes can interact with microbial membranes and biomolecules, while photoactivation can generate reactive oxygen species. Antibacterial PDT therefore provides an opportunity for spatially controlled microbial inactivation [10].

Future systems will need improved aqueous compatibility, selective microbial targeting, effective excitation wavelengths and low toxicity toward host cells. Combining antimicrobial action with luminescent detection may also permit simultaneous diagnosis and treatment.

8. Photocatalysis and Energy-Related Applications

The excited-state redox properties of Ru(II) polypyridyl complexes have made them valuable in photoredox chemistry. Applications include organic synthesis, oxidation and reduction reactions, hydrogen evolution, carbon-dioxide conversion and solar-energy-related processes [3,12].

The modularity of the ligand framework permits tuning of absorption and redox potentials. Multinuclear and supramolecular Ru(II) architectures provide additional opportunities for controlling energy and electron transfer [12]. A practical limitation is the cost and limited natural abundance of ruthenium, encouraging development of highly efficient systems and earth-abundant alternatives.

9. Structure–Activity Relationships

Table 4. Structure–property–application relationships

Structural modification	Expected effect	Potential application
π-Extended ligand	Red-shifted absorption; increased aromatic surface	PDT; DNA binding [5,8,9]
Planar aromatic ligand	Enhanced π-stacking	DNA intercalation [1,5]
Hydrophilic substituent	Improved aqueous compatibility	Biological applications [2]
Lipophilic substituent	Increased membrane interaction	Cellular uptake [2]
Targeting group	Selective localization	Targeted therapy [2,7]
Photolabile ligand	Light-triggered activation	Photoactivated chemotherapy [2,8]
Multiple Ru centres	Enhanced electron / energy transfer	Photocatalysis [12]
Two-photon absorbing ligand	Deeper optical activation potential	Imaging; PDT [8,9]

Sources: Numbered references correspond to the reference list in the review manuscript.

The performance of Ru(II) polypyridyl complexes is governed by a combination of metal-centre properties and ligand architecture. Extended aromatic surfaces generally favour DNA association, while positive charge promotes electrostatic interactions. Lipophilic groups can enhance membrane association but may also alter nonspecific binding. Hydrophilic groups can improve aqueous compatibility. π-expansion can shift optical properties and influence excited-state behaviour [2,5,9].

These relationships emphasize the need to optimize biological activity and photophysical performance simultaneously rather than treating them as independent properties.

10. Current Challenges and Future Prospects

Major challenges include selective delivery, pharmacokinetics, tissue penetration, hypoxic tumour environments and long-term toxicity. Near-infrared excitation and two-photon activation may improve the practical utility of phototherapeutic systems [9]. Targeting groups, peptides and nanomaterials can be used to improve cellular or organelle selectivity [2].

The next generation of complexes is likely to integrate several functions within one molecular platform: targeting, imaging, sensing, photoactivation and therapy. Such multifunctional systems could provide improved spatial control and enable real-time monitoring of therapeutic response.

11. Conclusions

Ru(II) polypyridyl complexes have evolved from fundamental photochemical systems into versatile platforms for DNA recognition, imaging, therapy, antimicrobial treatment, sensing and photocatalysis. Their major strength lies in the ability to tune molecular properties through ligand design while retaining favourable ruthenium coordination chemistry.

Future advances should focus on rational structure–activity relationships, long-wavelength activation, targeted delivery, oxygen-independent photochemistry and comprehensive biological evaluation. The convergence of molecular recognition, photophysics and therapeutic activity makes Ru(II) polypyridyl chemistry a particularly promising area for interdisciplinary research.

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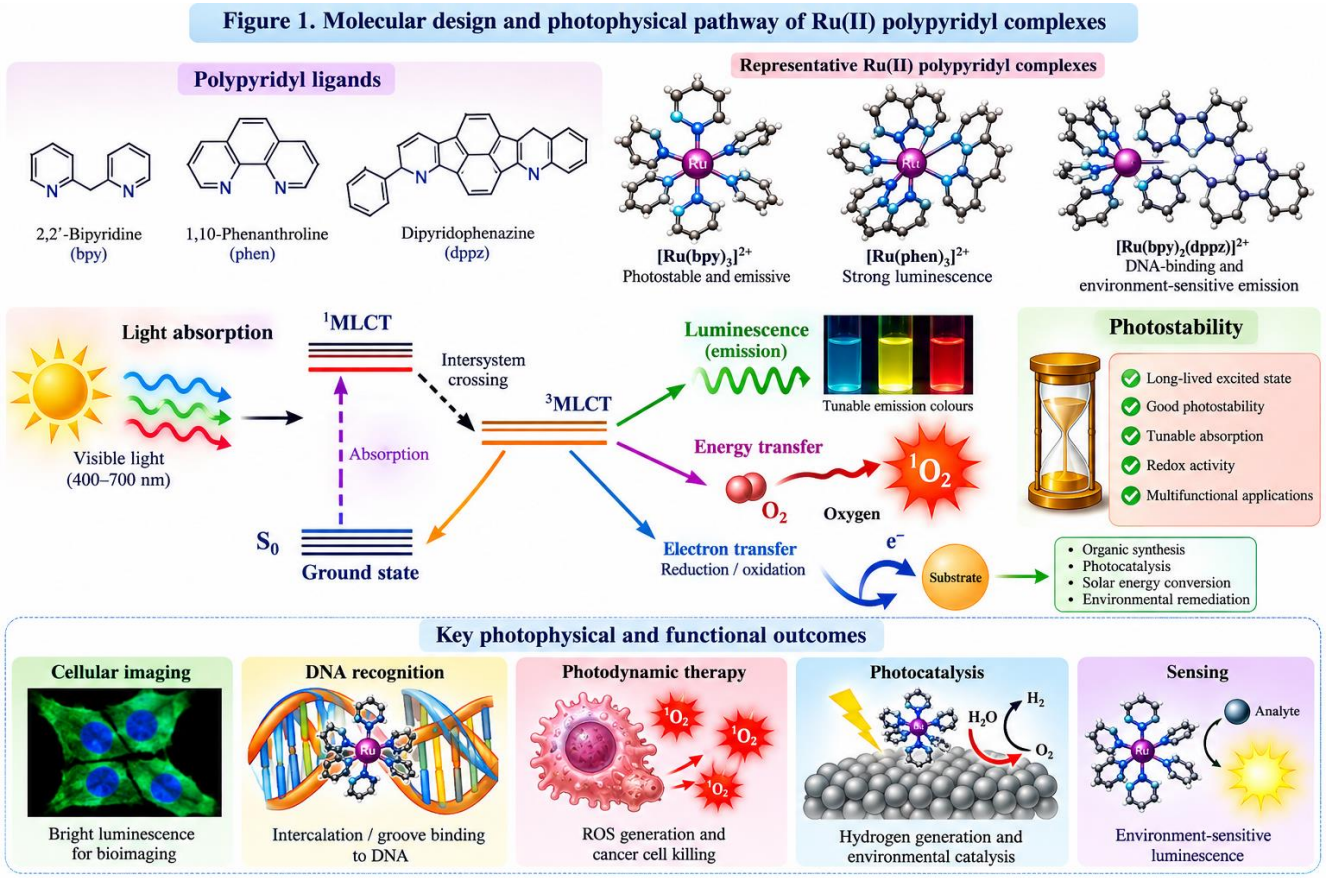

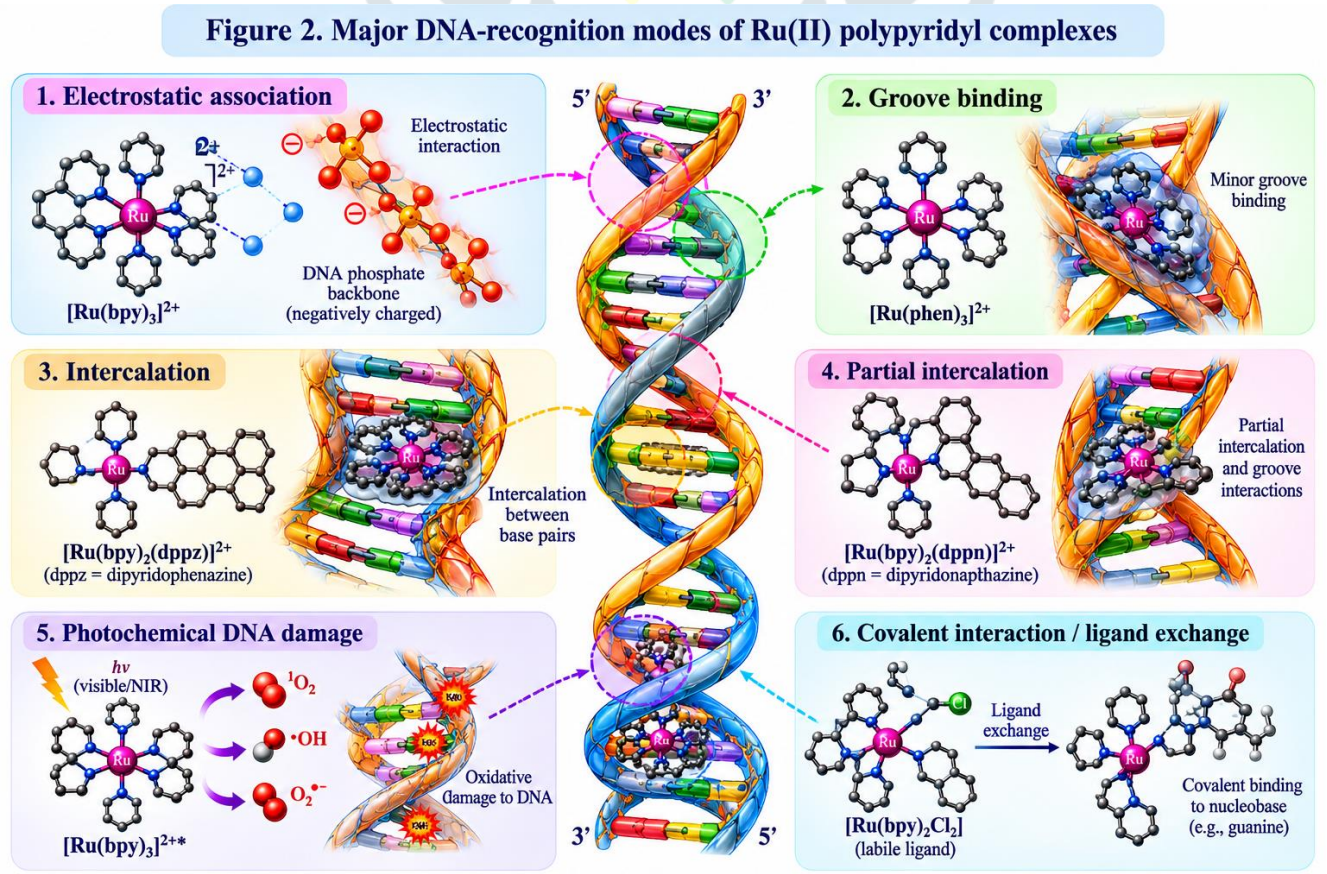

3. DNA Recognition section.

Figure 3. Multifunctional biomedical applications of Ru(II) polypyridyl complexes

