



ANTIBACTERIAL PHOTODYNAMIC ACTIVITY AND SYNERGY OF RUTHENIUM(II) COMPLEXES WITH POLYMYXIN B/PHENYLALANINE-ARGININE β -NAPHTHYLAMIDE AGAINST CLINICALLY RELEVANT BACTERIA



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Introduction

Aim:

In recent years, photodynamic therapy (PDT) has emerged as potential alternatives in combating the growing threat of global antibiotic resistance. In PDT, free radicals are generated in the presence of photosensitizers and oxygen under light irradiation of specific wavelength, causing cytotoxic damage to bacteria. The objective of this study is to investigate the potential of synthesised ruthenium, Ru(II) complexes as antibacterial photosensitisers and antibiotic adjuvants.

Hypothesis:

Ru(II) complexes are potent antibacterial PDT agents and combination of Ru(II) complexes with either phenylalanine-arginine beta-naphthylamide (PA β N) or polymyxin B sulfate (PMX) against susceptible and resistant strains of *Pseudomonas aeruginosa* (PA) and *Staphylococcus aureus* (SA) will enhance antibacterial activity.

Methodology:

Two Ru(II) complexes (Complex 1 and Complex 2) have been prepared and characterised. Their minimum inhibitory concentrations (MIC) ranging from 0.125-128 μ M were determined against SA and PA using broth microdilution method. Following that, checkerboard method was used to generate combinations of Ru(II) complexes with PMX and PA β N respectively against susceptible (S) and resistant (R) strains of bacteria. The fractional inhibitory concentrations (FIC) were also determined.

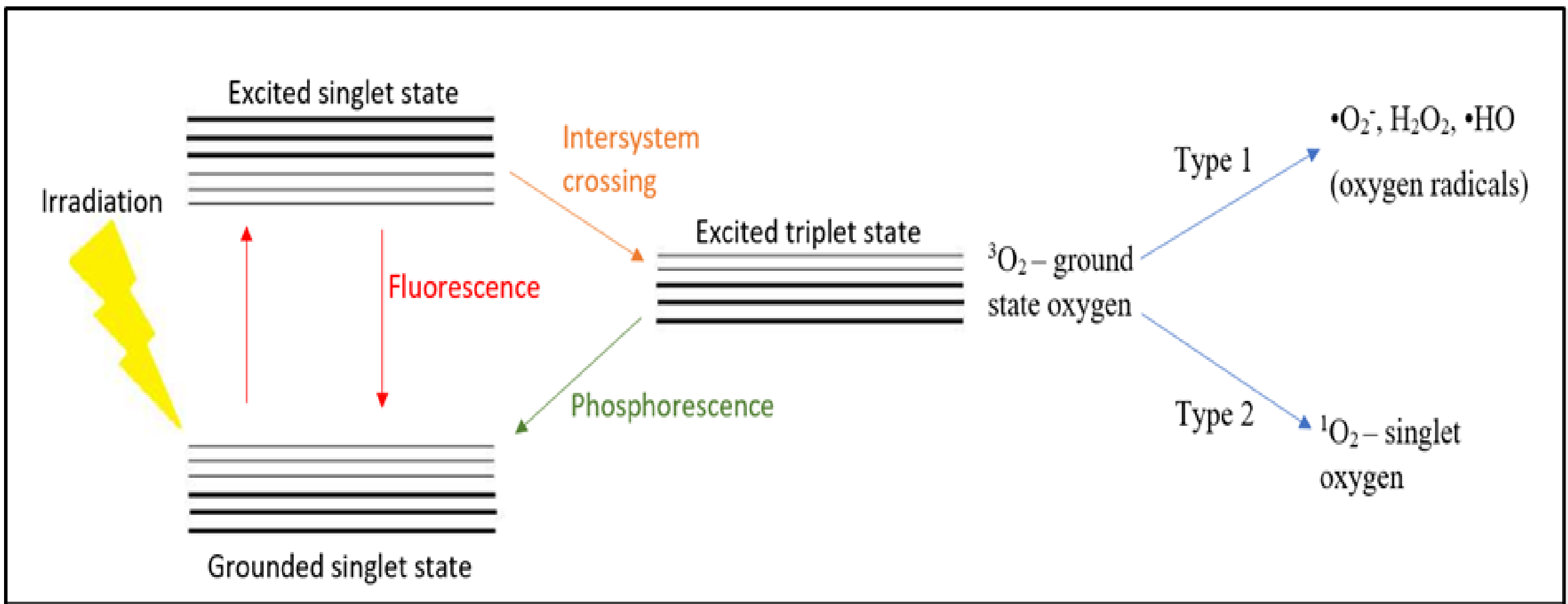
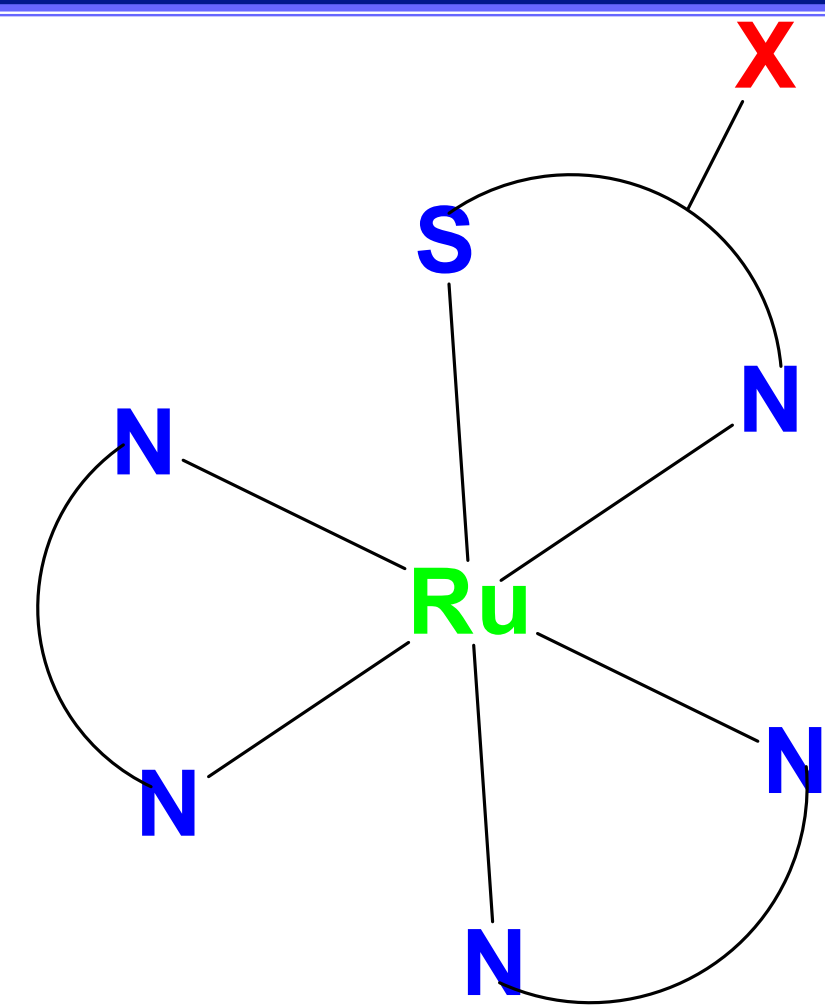


Figure 1: Photochemical and photophysical mechanisms of PDT involving Type 1 and Type 2 photodynamic therapy.



X = orthogonal reactive functions
N-N = polypyridyl ligands
N-S = Schiff base ligand

Figure 2: General structures of Complexes 1 and 2, with Complex 2 differs from Complex 1 in possessing an additional -OH group.

Results and Discussion

MIC determination

Compounds	Irradiated	Minimum Inhibitory Concentration (MIC) (μ M)			
		SA (R) ATCC 43300	SA (S) ATCC 35923	PA (R) ATCC BAA-2108	PA (S) ATCC 27853
Complex 1	Yes	16	16	>128	>128
	No	16	32	>128	>128
Complex 2	Yes	64	64	64	>128
	No	32	16	128	>128
PMX	Yes	>128	>128	1	0.125
	No	>128	>128	0.5	0.5
PA β N	Yes	>128	128	>128	>128
	No	>128	128	>128	>128

Table 1: Individual MIC of complexes 1 and 2

Σ FIC determination

Bacteria	Irradiated	Σ FIC range (Σ FICmin and Σ FICmax)			
		Combination with PMX		Combination with PA β N	
		Complex 1	Complex 2	Complex 1	Complex 2
SA (S)	Yes	0.516-1.000	0.375-0.750	0.625-1.000	0.500-0.750
	No	0.188-0.625	0.750-1.000	0.250-0.625	0.625-1.000
SA (R)	Yes	0.500-0.750	0.141-0.625	0.625-1.000	0.258-0.625
	No	0.375-0.750	0.188-0.625	0.500-0.750	0.258-0.625
PA (S)	Yes	NA	NA	NA	NA
	No	0.375-0.625	NA	NA	NA
PA (R)	Yes	0.281-0.750	0.129-0.254	0.501-1.000	NA
	No	0.563-1.000	0.252-0.502	0.508-1.000	NA

Table 2: Calculated Σ FIC range of combinations with PMX and PA β N

Conclusion

- The Ru(II) complexes showed potential as antibacterial PDT agents in which the compounds exhibit higher antibacterial activities upon irradiation.
- Combinational therapy demonstrated promising synergistic and additive effects when combining the metal complexes with either PA β N or PMX.

References

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