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Novel nitro phenanthroline-based ruthenium complexes as the promising antimicrobial agents.

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Multidrug resistance of bacterial pathogens is a major health concern worldwide, and there is an urgent need for the development of new and effective antimicrobial agents[1]. Considering the pharmacological potential of metal-based compounds[2], a new ruthenium(II) compound *cis*-[Ru(phen)$_2$(4-bzpy)(NO$_2$](PF$_6$) was synthesized and characterized by spectroscopic and electrochemical techniques. The structure was determined by nuclear magnetic resonance. The photochemical behavior in aqueous solution demonstrates that upon irradiation with blue light (453 nm), a photochemical reaction occurs, converting the nitrite (NO_2) ligand into nitric oxide (NO). The progress of NO photo-release was monitored using differential pulse voltammetry. The anodic process observed at 0.80 V was assigned to the oxidation of the released NO^0. This complex also showed promising antibacterial activity against a Gram-positive bacterial strain, specifically Staphylococcus aureus and Staphylococcus epidermidis (See table 1). To verify any damage as a consequence of DNA binding, we performed agarose gel electrophoresis of the pBR322 DNA mixed with complex under irradiation with blue LED (λ_{irr}=453 nm) or incubated in the dark. Interestingly, the title complex, in the dark, did not show any evidence of DNA cleavage even with up to 80 µM of this metal complex. On the other hand, under blue light irradiation, this ruthenium complex promoted efficient DNA cleavage, leading up to formation of nicked DNA (form II). Corroborating with these results, we observed that the antimicrobial activity of the complex was enhanced upon blue LED irradiation which may be related to the release of NO. These results suggest that the increased antimicrobial activity might be related to DNA damage, as indicated by electrophoresis studies.

Table 1. Minimum inhibitory concentrations (MIC) and minimum bactericidal concentrations (MBC) of ruthenium complex against bacteria.

Compound *cis*-[Ru(phen)$_2$(4-Bzpy)NO$_2$]$^+$	Blue LED		*S. aureus* ATCC 25923	*S. aureus* ATCC 700698	*S.aureus JKD*	*S. epidermidis* ATCC 12228
	ON	MIC	32	128	64	16
		MBC	32	256	64	128
	OFF	MIC	256	512	128	32
		MBC	512	-	256	128

*MIC and MBC are expressed in µg/mL. (-) Activity not detected for 500 µg/mL

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References

1. Reynoso, E. C., Laschi, S., Palchetti, I. & Torres, E. Advances in Antimicrobial Resistance Monitoring Using Sensors and Biosensors: A Review. *Chemosensors* **9**, 232 (2021).

2. Singh, S. *et al.* Photodissociation of nitric oxide from designed ruthenium nitrosyl complex: Studies on wound healing and antibacterial activity. *Nitric Oxide* **129**, 30–40 (2022).