Polypyridyl ruthenium(II) complexes as cytotoxic lipophilic cations: new paradigms for old molecules?

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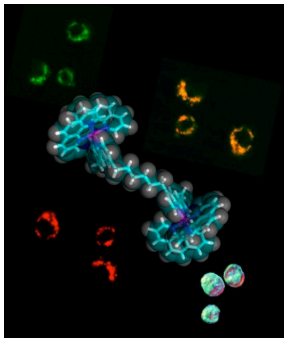
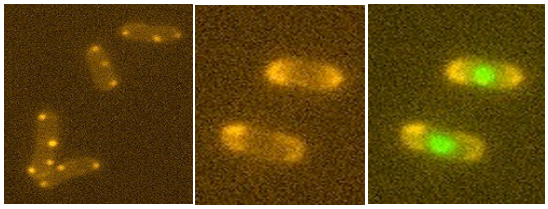
There has been considerable interest in the use of inert polypyridyl ruthenium(II) complexes for biological applications. The ability of such complexes to bind nucleic acids with some degree of specific sequence and structure recognition has highlighted their potential as diagnostic and therapeutic agents. In most cases, the cytotoxicity of the ruthenium(II) complexes has been attributed to their interactions with nucleic acids.[1]



We have synthesised a series of dinuclear ruthenium polypyridyl complexes where the two ruthenium centers are linked by a chain of 2-16 methylene groups: these species have a high affinity for non-duplex DNA structures,[1,2] and are highly cytotoxic to leukaemia cells where the cytotoxicity is proportional to chain length.[3] Interestingly, the DNA affinity trends show little correlation with the cytotoxic properties. A detailed study on their cytotoxicity, uptake mechanism and localisation has shown they act as highly cytotoxic lipophilic cations, entering the cell by passive diffusion (with a minor protein-mediated active transport component), poisoning the mitochondria and causing cell death by apoptosis.[3]

This genre of complexes also exhibited high levels of antimicrobial activity against a range of pathogens, including multi-drug resistant strains such as methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*.[4-6] However, they showed low levels of toxicity against human cell lines.[4]



The seminar will look at the synthesis of these compounds, their interactions with nucleic acids, cell uptake studies and aspects of their particularly significant antimicrobial behaviour.

References

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