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Silver-N-heterocyclic carbene complexes for anticancer applications

In recent years, metal-N-heterocyclic carbene (NHC) complexes have been investigated in biomedical applications, showing promise as antibacterial (silver-NHCs) and as anticancer (palladium-, copper-, gold- and silver-NHCs) agents.¹ An initial paper from my group highlights the effects of various silver-NHC complexes on cytotoxicity, with bidentate cationic silver-NHCs being more cytotoxic than their monodentate counterparts.² The work, which was a hot article in *Dalton Transactions*, was highlighted in *New Scientist* and attracted considerable media attention. More recent work uses NHC ligands that are derived from natural products such as caffeine, with a view to lowering the potential toxicity of the ligand component (Figure 1 A).³

Although silver-NHC complexes have shown considerable potential as anticancer drugs, and despite the supposed inherent low toxicity of silver (it is incorporated into several materials such as wound dressings, creams, deodorants and even clothing), this area has not been developed compared to other metals in cancer therapy. NHC ligands can be tuned to significantly alter the properties of silver complexes (e.g. solubility, stability, complex charge, biocompatibility), therefore are a perfect partner for silver to examine in cancer therapy. A major barrier to the continued development of these compounds is the lack of a defined mechanism of action or cancer specific target. We work in collaboration with Professor of pharmacology Roger Phillips to enable us to gain a mechanistic understanding of these complexes on cells, which allows a more systematic approach to their development. Furthermore, we are working with Dr Paul Thornton, a polymer chemist at Leeds, to develop delivery vehicles for these complexes as a means to stabilise the species in biological environments, and deliver the drug to the intended target.

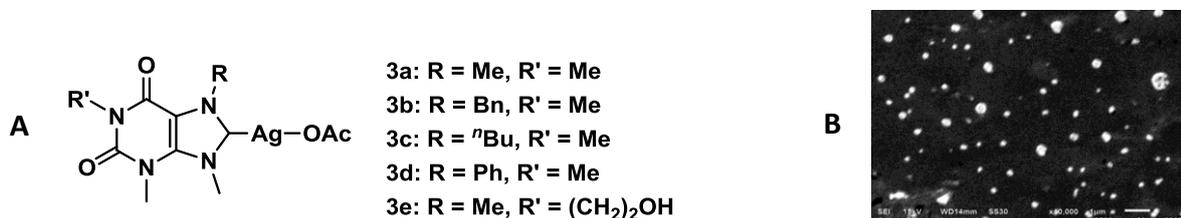


Figure 1 (A) Cytotoxic silver-NHC complexes.³ (B) Silver-NHCs incorporated into polymer micelles (Z-average = 121.4 nm, PDI = 0.26).

The student working on this project will gain a wide range of skills including in both organic and organometallic synthesis, polymer chemistry and in pharmacological techniques. A range of analytical skills will be developed including NMR and UV spectroscopy, mass spectrometry and single crystal X-ray diffraction.

Please contact Dr. Charlotte Willans (c.e.willans@leeds.ac.uk) for further details about this opportunity.

References

1. H. A. Mohamed and C. E. Willans, *Organometallic Chemistry* **2014**, 39, 26.
2. D. C. F. Monteiro, R. M. Phillips, B. D. Crossley, J. Fielden and C. E. Willans, *Dalton Transactions*, **2012**, 41, 3720.
3. H. A. Mohamed, B. R. M. Lake, T. Laing, R. M. Phillips and C. E. Willans, *Dalton Trans.* **2015**, 44, 7563.