Polynuclear Bioorganometallics:

Novel Strategies for Metal-Based Drugs.

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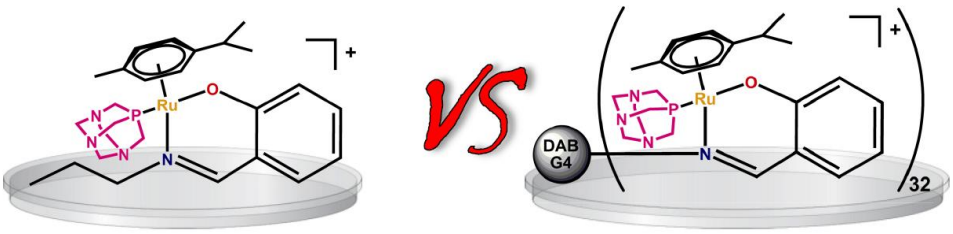
Keywords: bioorganometallics, polynuclear, metallodendrimers, anticancer, antimalaria.

Research into polynuclear bioorganometallic complexes as molecular tools in biological applications, particularly as chemotherapeutics is gaining prolific interest [1]. It is the multivalent nature of these materials, which leads to increased interactions between a drug conjugate and a target bearing multiple receptors, further improving the selectivity, in particular, towards cancer cells. Large macromolecules, like dendrimers, can also specifically target tumours by exploiting the 'enhanced permeability and retention' (EPR) effect, in which macromolecules can accumulate at the tumour site due to an increase in blood vessel permeability within diseased tissues compared to normal tissues [2]. Polynuclear metal-containing complexes offer the possibility of cooperative physical and chemical properties arising from interactions among the metal centres

As part of our continuing investigations into the synthesis of polynuclear organometallic macromolecules, we recently synthesised a series of multinuclear PGM complexes based on first- and second-generation poly(propyleneimine) dendritic scaffolds [3-5], which show a clear correlation between the size of the metallodendrimer and the cytotoxicity, with the higher generation, chelating, cationic metallodendrimers displaying enhanced activity.



This presentation reports on the synthesis of an extended series of polynuclear PGM (Ru, Rh, Ir) complexes based on poly(propyleneimine) dendritic scaffolds. The pharmacological evaluation of the complexes, as a function of the metal and varying co-ligands, as anticancer and antiplasmodial agents will also be discussed.

[1] Boas, U; Christensen, J.B.; Heegaard, P.M.H. *Dendrimers in Medicine and Biotechnology: New Molecular Tools*, RSC Publishing, 2006.

[2] Baban, D.F.; Seymour, L.W. *Adv. Drug Delivery Rev*. 1998, **34**, 109.

[3] Govender, P.; Renfrew, A.K.; Clavel, C.M.; Dyson, P.J.; Therrien, B.; Smith, G.S. *Dalton Trans*. 2011, **40**, 1158.

[4] Govender, P.; Sudding, L.C.; Clavel, C.M.; Dyson, P.J.; Therrien, B.; Smith, G.S. *Dalton Trans*. 2013, **42**, 1267.

[5] Payne, R.; Govender, P.; Therrien, B.; Clavel, C.M.; Dyson, P.J.; Smith, G.S. *J. Organomet.Chem.* 2013, **729**, 20