Spectroscopic & neutron scattering studies of model polymer therapeutics interacting with bioinspired model surfaces

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Abstract

The amphoteric, endosomolytic poly(amidoamine) (PAA) ISA23.HCl is able to cause pH-dependant red blood cell (RBC) lysis and has potential for gene delivery. Recently, it has also been shown to cause endosomal/lysosomal permeabilization when internalized by liver cells after administration in vivo. However, the efficiency is still rather low. Thus, to aid the design of more effective PAA chemistries we began to investigate the physicochemical properties of ISA23.HCl in those biological environments it would encounter during cellular uptake and intracellular trafficking. Techniques more commonly applied in colloidal science such as pulsed-gradient spin-echo NMR, electron paramagnetic resonance (EPR) and small-angle neutron scattering (SANS) were used to study solution conformation and model surface interaction.

(1) *K.W. Wan et al., Biomacromolecules 5 (2004) 1102;* ***(2)*** *P.C. Griffiths et al., Biomacromolecules 5 (2004) 1422;* ***(3)*** *Z. Khayat et al., Int. J. Pharm. 317 (2006) 175;* ***(4)*** *P.C. Griffiths et al., Biomacromolecules 8 (2007) 1004*

Biography

Peter Griffiths was awarded a PhD in 1991 for his research with Prof. Terence Cosgrove in quantifying the diffusion of probe or trace polymers through complex colloidal solutions using pulsed-gradient spin-echo (PGSE-NMR) NMR, a technique that now forms the cornerstone of his groups activities. He subsequently undertook a PDRA position in the same laboratory developing NMR and small-angle neutron scattering (SANS) methodologies to study concentrated colloidal dispersions. In 1994, he moved to Stockholm to work with Prof. Peter Stilbs to continue his application of PGSE-NMR to a novel range of colloidal problems, including thermoresponsive polymers, assessment of polydispersity and diffusion in gels. Peter was appointed Lecturer at Cardiff in 1995, Senior Lecturer in 2001/2 and subsequently Reader in 2004. Current projects within his group focus on probing the solution structure of bioresponsive copolymers for gene delivery and polymer-protein conjugates, as well as developing an understanding of the factors that govern the interaction of such polymer with common components found in biological media (proteins, lipids *etc*) and the impact of such polymeric species on well-defined model and biomimetic interfaces. PCG is founder and co-director of a centre of excellence – the "Centre for Applied Spin Resonance" - that provides access to- and expertise-of a range of spin-resonance methodologies, available to all staff within Cardiff University. He has published approximately 100 peer reviewed scientific papers and contributed to several books.

Outside the University, Peter is the Chair of the SCI Colloid and Surface Science Group, Chair of the Rideal Committee, committee member of the SCI Awards Committee and Chair of the South East Wales Local Section of the RSC.