Experimental report

02/02/2016

Proposal: 9-13-574 **Council:** 10/2014

Title: Diffusion of active pharmaceuticalingredients in supra-molecular gels

Research area: Soft condensed matter

This proposal is a new proposal

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Samples: Ethylacetate D8 with 10% Ibuprofen sodium
7:3 D2O/Ethanol D6 with 5%, 10%, 20% Ibuprofen sodium
Ethylacetate D8 gels with 10% Ibuprofen sodium
7:3 D2O/Ethanol D6 gels with 5%, 10%, 20% Ibuprofen sodium

Instrument	Requested days	Allocated days	From	To
IN16B	4	4	23/07/2015	27/07/2015

Abstract:

Gels, i.e. solid-liquid colloids, consist of up to 99.9% liquid whilst exhibiting macroscopic characteristics of a solid. This makes them especially interesting in the context of pharmaceutical drug delivery. In order to characterise drug retention and release in these colloidal systems, we have investigated solvent diffusion in supramolecular gels by quasi-elastic neutron scattering on IN6 and LET and found that the solvent diffuses slightly more quickly in the gels than in the bulk solvent. Whilst this behaviour can be of great advantage, i.e. for modified release, it can also hinder the direct release of the drug, and thus has significant bearing on the practical application of drug delivery gels as well as being a fundamentally poorly understood phenomenon in these topical composite materials. Thus, we now propose to investigate the diffusion of drug molecules in pure solvent compared to that in supramolecular gels. We will investigate this in dependence of the temperature, gellator and drug concentration in two different solvents and thus ask for 4 days of beam time on IN16B.

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In our earlier experiments at IN6 (ILL) and LET (ISIS), we found that in a specific supra-molecular gel the solvent diffusion is quick than in the comparable bulk solvent. In this experiment on IN16b we aimed to investigate

- the diffusion of a model drug molecule in the supra-molecular gels and the corresponding pure solvents;
- whether the quicker solvent diffusion in the gels impacts the diffusion of the drug loaded into the gel. This would have implications on understanding supra-molecular gels for drug delivery.

We have measured following samples:

Sample	Temperature
7:3 water/ethanol (D/D)	265 K
0.3% w/w gel, 7:3 water/ethanol (D/D)	265 K and 270 K
20% IBU, 0.3% w/w gel, 7:3 water/ethanol (D/D)	265 K, 270 K and 290 K
20% IBU, 7:3 water/ethanol (D/D)	265 K
10% IBU, 0.3% w/w gel, 7:3 water/ethanol (D/D)	265 K and 270 K
10% IBU, 7:3 water/ethanol (D/D)	265 K and 270 K
0.5% w/w gel, 7:3 water/ethanol (D/D)	265 K and 270 K
10% IBU, 0.5% w/w gel, 7:3 water/ethanol (D/D)	265 K and 270 K
Ethylacetate (H)	220 K and 195 K

All samples were prepared following the same experimental procedure to ensure comparability between solution and gel samples.

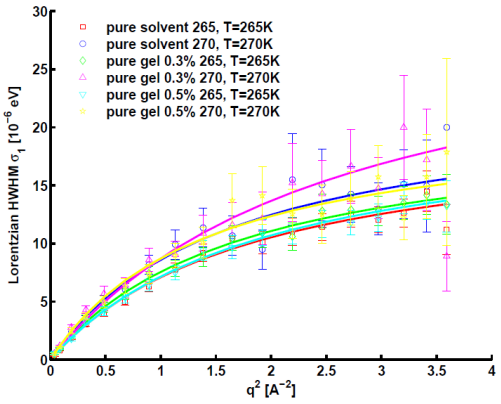

Figure 1 preliminary modelling of the pure solvent diffusion in bulk solvent and gel as modelled using a jump-diffusion model.

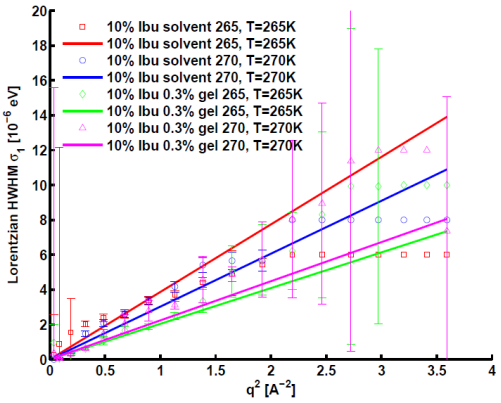

Figure 2 Preliminary modelling of ibuprofen sodium diffusion in bulk solvent and gel

Our preliminary data analysis shows that we can clearly quantify both the diffusion of the pure deuterated solvent and the solvent inside the gels (figure 1). The solvent diffusion can be linked to the existing LET and IN6 data. In this way, by combining the accessible dynamic windows of these

different spectrometers, we will in later, more advanced data analysis obtain more accurate numbers than in the preliminary fit depicted in figure 1of the IN16B unloaded solvent and unloaded gel data .

In a second step we have fitted the spectra recorded on IN16B on the pure solvents and gels loaded with the drug molecule Ibuprofen (as sodium salt). For these fits, we have fixed the Lorentzian line widths (but not the amplitudes) given in figure 1 corresponding to the deuterated solvent diffusion. A second Lorentzian was fitted with free amplitude and free width parameter without imposing any dependence on the scattering vector *q*. The fit results for this second Lorentzian width thus describing the diffusion of the Ibuprofen are consistent with a simple Brownian diffusion within the errors (figure 2). In the next step, we will improve the fits a using a more accurate model for the solvent diffusion from the combination of the IN6, LET and IN16B data.