Experimental report

08/02/2016

Proposal: 6-05-952 **Council:** 10/2014

Title: Study of the relaxational/vibrational dynamics of glass-forming systems of pharmaceutical interest

Research area: Physics

This proposal is a new proposal

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Samples: trehalose C12H22O11, glycerol C3H8O3

Instrument	Requested days	Allocated days	From	To
IN5	5	5	10/07/2015	15/07/2015

Abstract:

The carbohydrate trehalose and the alcohol glycerol, which are classified as intermediate in the Angell's strong-fragile scheme, are used as shelf-life extending additives in many labile pharmaceutical products. Since the preparation protocols used for obtaining the pharmaceutical systems affect the degree of crystallinity which plays a key role in determining the system stabilising properties and its bioprotective effectiveness, this is expected to have a significant role also in the understanding of the glycerol-trehalose mixture dynamical behaviour.
With the aim to characterize the relaxational/vibrational dynamics of the trehalose/glycerol mixture at a glycerol concentration value of 2.5% by weight, we propose to collect QENS data by the IN5B spectrometer on this mixture as obtained following two different preparation protocols, i.e. damage-formed as obtained by ball-milling and melt-formed as obtained by a rapid undercooling of the melted crystal:
- as a function of temperature across the glass transition temperature Tg at two different instrumental energy resolution values
and
- as a function of energy resolution at three temperature values above, below and at Tg.

EXPERIMENTAL REPORT

EXPERIMENT N° 6-05-952 INSTRUMENT IN5

DATES OF EXPERIMENT From : 10/07/2015 To : 15/07/2015

TITLE Study of the relaxational/vibrational dynamics of glass-forming systems of pharmaceutical interest

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In the present experiment we collected QENS data by the IN5B spectrometer on the trehalose/glycerol mixture at a glycerol concentration value of 2.5% by weight.
Trehalose (alpha-D-glucopyranosyl alpha-D-glucopyranoside, $C_{12}H_{22}O_{11}$, M_w=342.3 a.u., T_g=388K) and glycerol (1,2,3-propanetriol, $C_3H_8O_3$, M_w=92 a.u., T_g=190K) are classified as "intermediate" in the Angell's strong-fragile scheme [C. A. Angell, Science 294, 2335 (2001)] and are widely employed for the preservation of biomolecules [D. Wright, A. Eroglu, M. Toner, T. L. Toth, Reprod. BioMed. 9, 179, (2004)]. Furthermore, trehalose and glycerol are also used in mixtures as shelf-life extending additives in many labile pharmaceutical products [A. Simperler et al., Phys. Chem. Chem. Phys. 9, 3999 (2007)]. However the molecular mechanisms that determine their protective effectiveness are not fully understood yet.
Previous data collected on trehalose/glycerol (T/G) mixtures in a wide concentration range (0-20%) [S. Magazù et al., J. Chem. Phys. 132, 1845121 (2010); J. Phys. Chem. B 115, 11004 (2011); J. Non-Cryst. Sol. 358, 2635 (2012)] showed an unexpected behavior for the trehalose/glycerol mixtures as a function of the glycerol content, with a reduced mean square displacement, an enhanced rigidity and a slowing down of both the fast local dynamics and the diffusive dynamics at an estimated concentration value of about 2.5% by weight of glycerol in trehalose, suggesting a correlation between the suppression of the local fast dynamics and biostability [M. T. Cicerone, C. L. Soles, Biophys. J. 86, 3836 (2004)].
We performed the experiment taking advantage from the IN5B flexibility in the wavelength selection and chopper speed in order to choose different instrumental energy resolution

values, i.e. 10, 17, 30, 50, 100 and 300 μeV. Figure 1 shows the QENS spectra of the T/G mixture at 2.5% glycerol content at different temperature and resolution values.

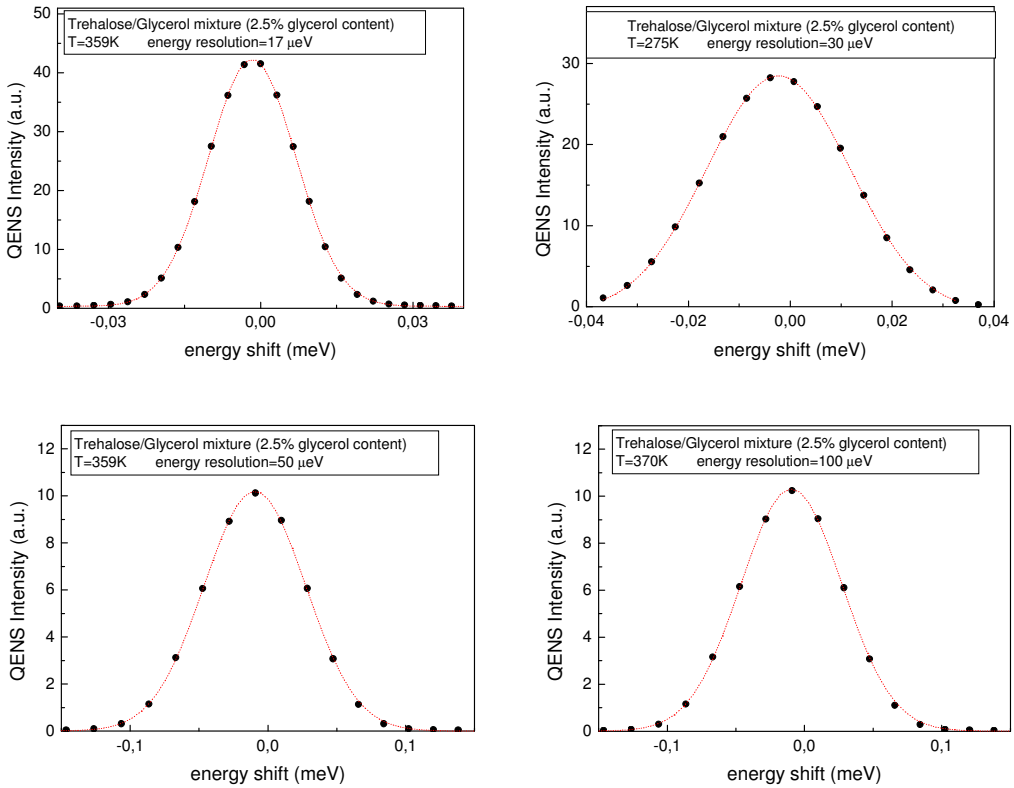

Figure 1. QENS spectra of the T/G mixture at a glycerol content of 2.5%

QENS data have been gathered at different temperature values in the range of 350÷370K for the energy resolution values, i.e. 10, 17, 30, 50, 100 and 300 μeV, at different temperature values in the range of 320÷390K at the energy resolution value of 50 μeV and at different temperature values in the range of 215÷390K at the energy resolution value of 30 μeV. In order to improve the data interpretation, we collected QENS data on glycerol at the temperature values of 215-255-295K at the energy resolution value of 10, 17, 30, 50, 100 and 300 μeV and on trehalose in the temperature range of 290÷359K at the energy resolution value of 30 μeV, at the temperature value of 359K at the energy resolution values of 10 and 17 μeV and in the temperature range of 320÷410K at the energy resolution value of 10 μeV. The complete analysis of the collected QENS data, with the evaluation of the intensity inflection points, i.e. the points where system relaxation time intersects the energy resolution time, is in progress. The elastic contribution should be evaluated as a function of temperature in a wide range of values in order to determine the dynamical transitions of the T/G mixture; however we were not able to register complete temperature runs due to beam-time restriction.