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Characterisation of Lactose in the Liquid and Solid State using Nuclear Magnetic Resonance and Other Methods

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Abstract

The anomeric composition of lactose is studied using polarimetry, gas liquid chromatography and a variety of nuclear magnetic resonance (NMR) methods and the results compared. As a result reliable characterisation based on solution methods is obtained. The measurement of the spectrum of nuclear spin-lattice relaxation times (T_1) of lactose powders demonstrate significant differences between crystalline and amorphous species and between the different crystalline forms of lactose. These differences form the basis of a new characterisation methodology of powdered lactose where measurements are performed in the solid state. The use of linear multi-exponential curve fitting algorithms (NNLS and Contin) to deduce the "relaxation spectrum" from the multiexponential decay curve (obtained using a low-cost wideline NMR machine) allows for the reliable interpretation of noisy and drift-affected inversion recovery data. The absence of spin-diffusion between crystalline and amorphous species enables the determination of the relative weight fractions of several lactose species in a mixed powder sample with a simple correlation to the relative intensities of relaxation time components of the T_1 spectrum. The T_1 values of amorphous lactose are shown to be sensitive to moisture content and the glass transition process. The quantitative results gained from using the T_1 method to characterise lactose can be applied to improve the functionality of lactose and lactose-containing powders.

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List of Symbols

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S : magnitude of the reciprocal space vector ($S = 2\sin\vartheta/\lambda$).
λ : wavelength of the X-rays.
$I_{cr}(S)$: coherent scattering intensity of the crystalline regions.
$I(S)$: coherent scattering intensity of the crystalline and amorphous regions.
$\overline{f^2}$: mean square amplitude of the atomic scattering factor.
D : disorder function.
k : disorder parameter.
X_{cr} : crystallinity of the material.
ΔH_{cr} : crystallisation enthalpy.

Chapter 3.

L : length of the polarimeter tube in decimeters.
c : anhydrous concentration of lactose in g/100 ml.
R_t : polarimeter reading at time t.
R_∞ : polarimeter reading at equilibrium.
$[R]$: the specific optical rotation.
w_∞ : weight of lactose sample used to determine R_∞.
W_a : anhydrous weight fraction.
α : percentage of alpha lactose present in the sample.
$[\alpha]$: specific optical rotation of alpha lactose.
$[\beta]$: specific optical rotation of alpha lactose.
$R_t^{'}$: normalised optical rotation reading.
E_a : activation energy.
R : universal gas constant.
T : temperature (in Kelvin).
A : pre-exponential factor.

Chapter 4.

H : Zeeman Hamiltonian operator.
γ : gyromagnetic ratio.
$\hbar$: $Plank's \quad constant(h)/2\pi$.

B_0 : polarising magnetic field.
$I_{x,y,z}$: angular momentum operator.
B_1 : oscillating magnetic field.
ω : frequency.
$U(t)$: evolution operator.
H_{rot} : Hamiltonian operator in the rotating frame.
$M_{x,y,z}$: components of the spin magnetisation vector, $\mathbf{M}$.
M_0 : magnitude of $M_z(t)$ as $t \to \infty$.
T_1 : spin lattice relaxation time.
T_2 : spin spin relaxation time.
μ_0 : permeability of free space.
$\mathbf{I}$: vector operator representing angular momentum.
$\mathbf{r}_{ij}$: internuclear vector.
r_{ij} : magnitude of the internuclear vector.
H_D : dipolar Hamiltonian operator.
W_{nm} : transition rate.
$E_{n,m}$: energies of states n and m.
i : $\sqrt{-1}$.
τ_c : average correlation time.
$J^{(q)}(\omega)$: spectral density function.
$\rho^*(t)$: density operator in the rotating frame.
$H_D^*(t)$: dipolar Hamiltonian operator in the rotating frame.
ω_0 : Larmor frequency.
$M(t)$: equal to $M_z(t)$
A_i : amplitude of component i.
$y(t_i)$: amplitude of multiexponential relaxation function at time t_i.
$s(T)$: unknown amplitude of relaxation time T.
t_i : time.
χ^2 : error function.
y_i : equal to $y(t_i)$.
$\dot{y}_i$: datum point.
σ_i : variance of datum points $\dot{y}_i$.
$\mathbf{x}_m$: column vector representing the true solution.
$\mathbf{x}$: column vector of the current estimate to $\mathbf{x}_m$.
$x_{i,j}$: components of the column vector $\mathbf{x}$.
$\mathbf{A}$: Hessian matrix.
$\mathbf{b}$: gradient vector.
$\mathbf{a}$: finite step required to find the minimum ($\mathbf{a} = \mathbf{x} - \mathbf{x}_m$).

$a_{i,j}$: components of vector **a**.
β_i : first partial derivative of χ^2 with respect to $\mathbf{x}$.
α_{ij} : second partial derivative of χ^2 with respect to $\mathbf{x}$.
$\mathbf{x}_{\mathbf{next}}$: next estimate of $\mathbf{x}$.
λ : constant.
s_j : spectral amplitude of component j.
T_j : relaxation time component j.
$\mathbf{Q}$: Householder transformation matrix.
$\mathbf{R}_k$: upper triangular matrix.
$\mathbf{u}$: an m vector
$\mathbf{u}^{\mathrm{T}}$: transpose of $\mathbf{u}$
μ : constant.
$\mathbf{H}$: matrix representing additional constraints used in continuum formulation.
$\mathbf{c}$: an n vector.
$M^{'}(t)$: corrected magnetisation.

Chapter 6.

C_p : heat capacity at constant pressure.
α_p : volume expansivity at constant pressure.
H : enthalpy.
V : volume.
p : pressure.
z : order parameter.
$w_{1,2}$: weight fraction of components 1 and 2.
T_g : glass transition temperature.
k : constant.
T_1 : spin lattice relaxation time.
μ_0 : permeability of free space.
γ : gyromagnetic ratio.
$\hbar$: $Plank's \quad constant(h)/2\pi$.
r_{ij} : average intermolecular distance.
I : angular momentum operator.
τ_c : average correlation time.
ω : frequency.
$\tau(T)$: mechanical and electrical relaxation time at temperature T.
$C_{1,2}^{g}$: arbitrary constants.

T_g : glass transition temperature.

$\phi_{CR,g}$: relaxation times of crystallisation at temperatures T and T_g respectively.

Chapter 7.

$M(t)$: amplitude of the inversion recovery signal at time t.

M_0 : amplitude of the inversion recovery signal at $t = 0$.

$A_{am,cr}$: relative amplitude of the amorphous and crystalline parts of the inversion recovery signal respectively.

T_{1CR} : spin lattice relaxation time of the crystalline part of the sample.