Molecular mobility on the crystalline state of a hypolipidemic drug: simvastatin

M. T. Viciosa[a], J. J. Moura-Ramos[a], H. P. Diogo[b], N. T. Correia[c], T. G. Nunes[b]
[a]*Centro de Química-Física Molecular,* [b]*Centro de Química Estrutural, Instituto Superior Técnico, 1049-001 Lisboa, Portugal*
[c]*REQUIMTE, Departamento de Química, Faculdade de Ciências e Tecnologia da Universidade Nova de Lisboa, 2829-516 Caparica, Portugal*
teresaviciosa@ist.utl.pt

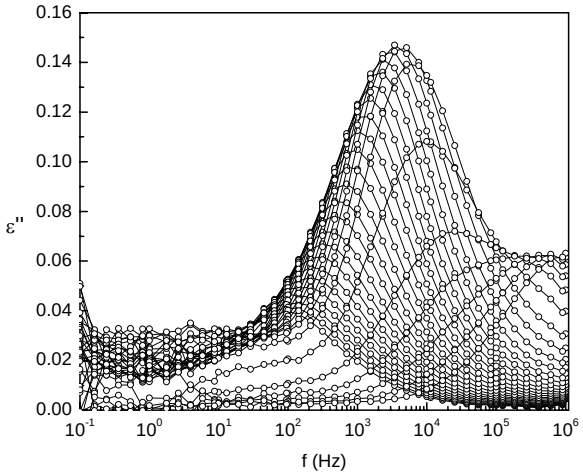

Figure 1. Dielectric loss spectra of simvastatin taken in the interval –90 to -30 ºC every 2 degrees.

Crystalline solids often undergo structural rearrangements in response to pressure and/or temperature. These so-called polymorphs have different physical and chemical properties, which can be relevant in areas ranging from pharmaceutical to dye and food industry. In the particular case of simvastatin, a cholesterol-lowering agent commonly used to treat hypercholesterolemia, three polymorphs have been identified with well-defined temperature regions (enantiotropic system). The main difference between the three solid phases is attributed to a disordered part of the side chain ethyl group [1].

The objective of the present study was to investigate the slow molecular movements of this model drug in two different crystalline forms. With this aim, two dielectric techniques were used: Dielectric Relaxation Spectroscopy (DRS) (Fig. 1) and Thermal Stimulated Depolarization Currents (TSDC). The results indicated that below T= -40 ºC (phase III) two noncooperative processes exist with similar activation energies; in the temperature interval -40 ºC < T < +2 ºC (phase II), one of the process splits into two with very different temperature behaviors. The evolution with temperature of the dielectric strength and the relaxation times for each process, obtained from DRS and TSDC studies, will help to discuss the origin of the molecular motions in the crystalline phases of simvastatin. Our results will be compared with literature data obtained from ss-NMR and synchrotron powder diffraction studies [1]. Additional Differential Scanning Calorimetry (DSC) was also used to determine the transition temperatures between polymorphs and to the entropy change associated. The low values of ΔS estimated confirm that both crystalline forms can be identified as plastic crystal forms.

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References: [1] M. Hušák, B. Kratochvíl, A. Jegorov, J. Brus, J. Maixner, J. Rohlíček, Structural Chemistry 21 (2010) 511-518.