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Biochemistry Project Report

Study of the crystallization kinetic of the racemic drug flurbiprofen by differential scanning calorimetry and dielectric relaxation spectroscopy

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Abstract

The goal of this work was to apply Dielectric Relaxation Spectroscopy (DRS) and Differential Scanning Calorimetry (DSC) to investigate the crystallization behavior of the drug racemic flurbiprofen, a low molecular weight glass former. The kinetic of isothermal crystallization was monitored during the occurrence of melt-crystallization and cold-crystallization. As a supplementary technique Polarized Optical Microscopy (POM) was used.

The results obtained by DSC and DRS show that flurbiprofen exhibits a glass transition ($T_{g,DSC}$=-6ºC) and crystallizes at higher temperatures. For a heating rate of 10ºC/min by calorimetric measurements, it is clearly observed the conversion between different crystalline forms (I and II), giving sign that flurbiprofen exhibits polymorphism. The observation obtained by POM permitted to physically visualize this crystalline transformation. Furthermore, the melting temperature of form I was determined as 115ºC.

Following the isothermal crystallization of form II either by DRS and DSC allowed extracting kinetics information. It was found that crystallization rate increases with increasing temperatures, in the temperatures studied (16ºC, 20ºC and 24ºC).

Dielectric relaxation and Differential Scanning Calorimetry proved to be suitable tools to study the molecular mobility and crystallization features of a glass former as racemic flurbiprofen. Although the glass transition and existence of polymorphism was already known in literature, the monitoring of isothermal crystallization in racemic flurbiprofen by DSC and DRS is reported by the first time.

Resumo

O objetivo deste trabalho foi aplicar a Espetroscopia de Relaxação Dielétrica (*DRS*) e Calorimetria de Varrimento Diferencial (*DSC*) na investigação do comportamento de cristalização do fármaco flurbiprofeno racémico, um formador de vidro de baixo peso molecular. A cinética de cristalização isotérmica foi monitorizada durante a cristalização vinda do fundido (*melt-crystallization*) e vinda do estado vítreo (*cold-crystallization*). Como técnica complementar foi utilizada Microscopia Ótica de Luz Polarizada (*POM*).

Os resultados obtidos por *DSC* e *DRS* evidenciaram que o flurbiprofeno exibe transição vítrea ($T_{g,DSC}$=-6ºC) e cristaliza a altas temperaturas. Para uma velocidade de aquecimento de 10ºC/min por ensaios calorimétricos é claramente observada a conversão entre diferentes formas cristalinas (I e II), dando sinal que o flurbiprofeno exibe polimorfismo. A observação obtida por *POM* permitiu visualizar fisicamente a transformação cristalina. Para além disso, a temperatura de fusão da forma I foi determinada como sendo 115ºC.

O seguimento da cristalização isotérmica da forma II quer por DRS quer por DSC permitiu extrair informação relativamente à cinética. Descobriu-se que a velocidade de cristalização aumenta com o aumento da temperatura, às temperaturas estudadas (16ºC, 20ºC e 24ºC).

As técnicas de relaxação dielétrica e de calorimetria de varrimento diferencial provaram ser ferramentas adequadas para estudar a mobilidade molecular e as características de cristalização de um formador de vidro como o flurbiprofeno racémico. Apesar da transição vítrea e da existência de polimorfismo serem já conhecidas na literatura, a monitorização da cristalização isotérmica do flurbiprofeno racémico por *DSC* e *DRS* é reportada pela primeira vez.