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A Comprehensive Spectroscopic Study of the Polymorphs of Diflunisal and their Phase Transformations

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Abstract

Understanding phase transitions in pharmaceutical materials is of vital importance for drug manufacturing, processing and storage. In this paper we have carried out comprehensive high-resolution spectroscopic studies on the polymorphs of the non-steroidal anti-inflammatory drug diflunisal that has four known polymorphs, forms I – IV (FI – FIV), three of which have known crystal structures. Phase transformations during milling, heating, melt-quenching and exposure to high relative humidity were investigated using Raman and terahertz spectroscopy in combination with differential scanning calorimetry and X-ray powder diffraction. The observed phase transformations indicate the stability order FIII > FI > FII, FIV. Furthermore, crystallization experiments from the gas phase and from solution by fast evaporation of different solvents were carried out. Fast evaporation of an ethanolic solution below 70 °C was identified as a reliable and convenient method to obtain the somewhat elusive FII in bulk quantities.

Keywords: diflunisal, phase transformation, polymorphs, terahertz spectroscopy

Chemical Compounds

Diflunisal (PubChem CID: 3059)