Comptes Rendus Chimie
Available online 10 October 2019
In Press, Corrected Proof

Full paper/Mémoire

Evaluation of the intermolecular interactions and polymorphism of mefenamic acid crystals in *N*,*N*-dimethyl formamide solution: A molecular dynamics simulation and experimental study

Siti Kholijah Abdul Mudalip [a, b], Fatmawati Adam [a, b], Mohd Rushdi Abu Bakar [c]

[a] Faculty of Chemical & Natural Resources Engineering, Universiti Malaysia Pahang, Lebuhraya Tun Razak, 26300 Kuantan, Pahang, Malaysia
[b] Centre of Excellence for Advanced Research in Fluid Flow (CARiFF), Universiti Malaysia Pahang, Lebuhraya Tun Razak, 26300 Kuantan, Pahang, Malaysia
[c] Industrial Pharmacy Research Unit, Department of Pharmaceutical Technology, Kulliyyah of Pharmacy, International Islamic University Malaysia, Bandar Indera Mahkota, 25200 Kuantan, Pahang, Malaysia

Received 31 May 2019, Accepted 16 August 2019, Available online 10 October 2019.

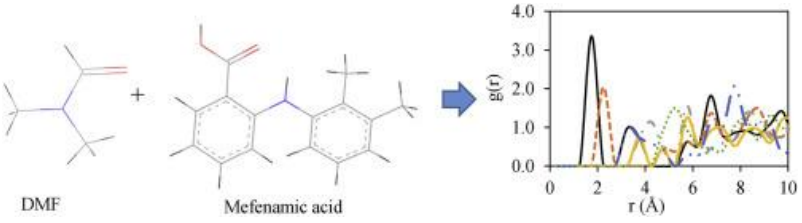
https://doi.org/10.1016/j.crci.2019.08.005

Abstract

Mefenamic acid [2-(2,3-dimethylphenyl)aminobenzoic acid] has been known to exist in different polymorphic forms. This study investigates the polymorphism of mefenamic acid in *N*,*N*-dimethyl formamide (DMF) through the combination of molecular dynamic simulations and experimental study. The molecular dynamic simulations were performed using the Material Studio 5.5 simulation package with a Condensed-phase Optimized Molecular Potentials for Atomistic Simulation Studies (COMPASS) force field. The simulation trajectory files were analyzed for radial distribution functions to investigate the intermolecular interactions. The experimental study was performed by the cooling crystallization method with DMF as the solvent. The saturated solution and crystals produced were analyzed by Fourier transform infrared spectroscopy, X-ray powder diffractometry, and scanning electron microscopy. The radial distribution function results showed the formation of a strong hydrogen bond between the solute–solute and solute–solvent interfaces, which were O1MA···H5MA and O_F···H15MA, respectively. The Fourier transform infrared results revealed the existence of O–H, N–H, and C═O bonds, which contributed to the formation of a hydrogen motif in the mefenamic acid during crystallization with DMF as the solvent. The X-ray powder diffractometry and scanning electron microscopy results confirmed the formation of mefenamic acid form II crystals in cubic shape.

Graphical abstract

Crystallization using different solvents may produce crystals with different polymorphic forms. The intermolecular solute–solute, solute–solvent, and solvent–solvent interactions existing in the solution control the self-assembly of mefenamic acid molecules and result in the formation of different polymorphs.



Keywords

Mefenamic acid; Molecular dynamic simulation; Hydrogen bonding; Solubility; Polymorphism; FTIR spectroscopy

Recommended articles Citing articles (0)

View full text