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Investigating the role of molecular interactions in polymorphism of mefenamic acid in ethyl acetate solution (Article)

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Abstract

View references (27)

Mefenamic acid, a widely used nonsteroidal anti-inflammatory and analgesic agent, is one of the active pharmaceutical ingredients that exhibit polymorphisms. This study reports a combined experimental and molecular dynamics simulation study of mefenamic acid crystallization in ethyl acetate. The solid-state characterization of the polymorph produced using Fourier transform infrared spectroscopy (FTIR), X-Ray powder diffractometer (XPRD), and differential scanning calorimetry (DSC) analysis show the characteristic of Form I, which were N-H stretching at 3313cm^{-1}, two endothermic peaks, and significant XPRD peaks at 6.3°, 13.8°, 15.9°, 21.3°, and 26.3°. The molecular dynamics simulations were performed using COMPASS force field available in the Material Studio 5.5 simulation package. The simulations were run for equilibration with a time step of 1 fs for a period of 250 ps and 2000 ps simulation in NVE (constant number of atoms, volume and energy) and NPT (constant number of atoms, pressure and temperature) thermodynamic ensemble, respectively. The trajectory files from the simulation were analyzed for radial distribution function (RDF) to investigate the intermolecular interactions. The simulation results showed strong solute-solute and solute-solvent interactions, which were O1MA•••H15MA and O1EA•••H15MA. These findings revealed the presence of hydrogen bonds that contributes to the solvation and formation of hydrogen motif in polymorphic Form I of mefenamic acid during crystallization with ethyl acetate as a solvent.

Reaxys Database Information

View Compounds

Author keywords

COMPASS Crystallization Hydrogen bonding Mefenamic acid Molecular dynamics simulation

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