Intermolecular interactions in solid drugs – what can high-pressure techniques contribute to their study?

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Intermolecular interactions play an important role in crystallization of drugs, in their solid-state reactivity and in their properties, including solubility, stability, heat capacity, bioavailability, mechanical properties, etc. It is important to understand intermolecular interactions, if one aims to optimize manufacturing, to control stability, to maximize bioavailability of drugs.

The contribution gives a few illustrations of the interrelation between the intermolecular interactions and the properties of solid drugs. It summarizes briefly several approaches to studying intermolecular interactions in drugs, ranging from thermoanalytical, spectroscopic, diffraction experimental techniques to database statistical analysis and computer simulations.

A special attention is payed to X-ray diffraction and vibrational spectroscopy at high hydrostatic pressures. To illustrate, what can high pressure studies contribute to the understanding of intermolecular interactions in molecular crystals, several examples are considered. Data on the effect of pressure on a number of molecular and ionic-molecular crystals: monoclinic (I) and orthorhombic (II) polymorphs of paracetamol, fenacetin, monoclinic (α) and trigonal (γ) polymorphs of glycine, *p*-benzoquinone, Co(III)-nitro- and nitrito-pentaammine complexes, sodium oxalate. A special attention is payed to the role of intermolecular interactions, in particular – hydrogen bonds - in the anisotropy of structural distortion. The high-pressure and low-temperature data are compared for the same compounds.

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