Poster Presentation

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Study of structural response of chlorpropamide polymorphs to external stress

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Polymorphism in molecular crystals is a remarkable property of Nature to create a wide range of various combinations of limited amount of components. Studies of the polymorphic crystals upon different types of external influence could be very useful in terms of analysis of molecular packing, nature and dynamics of the intermolecular interactions. When applied to pharmaceuticals, crystal structure may noticeably affect on stability, solubility, bioavailability, etc. which are essential for drug development. Sulfonyl urea derivatives represent a great example of compounds which are potentially inclined to conformational polymorphism. In particular generation drug chlorpropamide could be crystallized in a five different polymorphs. Chlorpropamide molecule is highly flexible in the crystal structure whereby we obtain various types of molecular conformations and their relative arrangements within the main structural forming motif – directed hydrogen bonded chains. Although polymorphic properties of chlorpropamide have been well-known for a decade there are still a lot of open questions regarding relative stability and crystallization conditions of the polymorphs as well as their behavior under extreme conditions such as cryogenic temperatures, hydrostatic pressure and mechanical stress. In order to follow dynamics of molecular fragments and to observe possible phase transitions on cooling and compression polarized Raman spectroscopy was used. Low temperature spectra were recorded in a wide temperature (5-300 K) range. The effect of hydrostatic pressure was studied using diamond anvil cell up to 5 – 5.5 GPa. Nanoindentation was applied to five polymorphs of chlorpropamide to examine and compare their mechanical properties. Experimental results were also supported by quantum-mechanical calculations. The research was supported by a grant for Russia-Slovenia collaboration BI-RU-12-13-038, a grant from RFBR and the Integration project 108 of the SB RAS.

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