

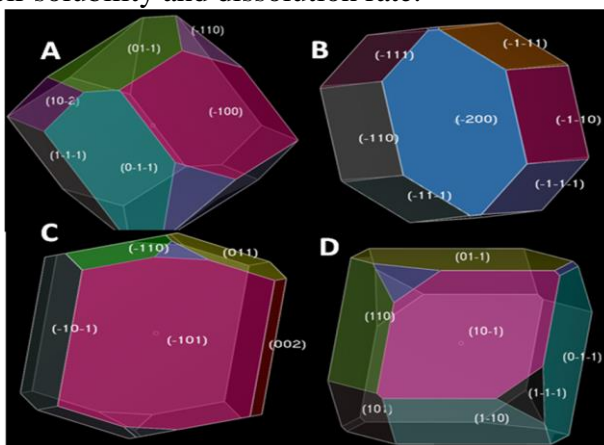
Structural Insight into Impact of Polymorphism on Vacuum Morphologies and Solubility Prediction of Felodipine Form IV

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Morphology is considered as the most evident characteristic of a crystal for the crucial identification of polymorphs, where the crystal structures vary only in terms of molecular arrangement at specified positions. In this paper, the impact of polymorphism on vacuum morphology was studied for a calcium channel blocker; felodipine. Felodipine was selected as a model drug to perform morphology comparison among its four different reported polymorphs using molecular simulations tools (Material Studio 6.1). An attempt was also made to correlate the structural properties with two important bio-pharmaceutical properties, namely solubility and intrinsic dissolution rate (IDR) and predict these properties for form IV polymorph which hitherto was not reported. BFDH, morphology growth and equilibrium morphology were included in the models for comparing the morphologies (COMPASS force field). The most important face with highest surface area obtained for felodipine polymorph I was (0 1 1), for polymorph II (1 1 0), for polymorph III (1 0 -1) and for polymorph IV (0 1 1). Correlations between the solubility and IDR with various simulated crystal morphological parameters like BFDH aspect ratio, morphology growth aspect ratio, entropy, attachment energy, surface energy and polar/non polar ratio were obtained for the three reported polymorphs. The highest solubility of form II was explained from its morphology and dominance of polar functional groups on crystal facets. The reported polymorphs for all the values showed a rank order correlation of II > I > III for various properties studied with correlated well with their reported solubility and IDR. Based on the established correlations, the solubility and IDR for form IV was calculated. This kind of research work can be helpful in predicting the impact of surface structure chemistry of polymorphs specifically which are difficult to crystallize on their solubility and dissolution rate.



A - BFDH Form I
B - BFDH Form II
C - BFDH Form III
D - BFDH Form IV

References

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