Virtual Cocrystal Screening

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Importance of cocrystals

Active pharmaceutical ingredients (APIs) are extremely valuable materials that are most conveniently developed and delivered as solid dosage forms. As low aqueous solubility of a drug can delay or limit its absorption in vivo, solubility enhancement has been one of the top priorities for decades in the pharmaceutical industry.[1] Pharmaceutical cocrystals raise important intellectual[2] and physical property issues in the context of drug development and delivery. Diversifying the number of crystal forms that exist for a particular API, cocrystals can lead to improvements in physical and chemical stability as well as mechanical properties. They can enhance the solubility, bioavailability, stability and dissolution rates of API crystal forms.[3]

Approach

Ab initio methods are used to predict the properties of non-covalent interactions in solution from molecular electrostatic potential surfaces of cocrystal components. The method can be applied to predict important thermodynamic properties such as solvation energy and free energy of complexation.[4] This approach is used in the identification of new cocrystal forms based on three predictions:

- The selection of potential cocrystal formers (CCFs)
- The experimental conditions that lead to cocrystal formation
- The impact of additives on the solubility of API's

The main advantage of this approach is that estimation of the free energy can be done directly from the gas phase *ab initio* calculations, without the need for empirical parameterisation.[5]

References

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