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Insights in the solubility and dissolution rate determination of cocrystals

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The formulation of pharmaceutical drugs in the form of cocrystals has experienced important advances in the last decade through the discovery of thousands of cocrystals. In fact, cocrystals can modify the physical properties of drugs, such as stability, melting point, solubility, and dissolution rate, without altering the pharmacological effect of the drug candidate. This make them a very attractive formulation alternative, especially for those drugs that have very poor aqueous solubility and low dissolution rate.
In this work we present two diferent case studies based on the solubility and dissolution improvement of two drugs (norfloxacin and adefovir dipivoxyl) when formulated as cocrystals. On one hand, norfloxacin, a poorly soluble fluoroquinolone antibiotic, has been formulated as a cocrystals using resorcinol as coformer. The cocrystal shows an improved solubility compared to norfloxacin itself. However, solid state state transformations occur during the course of solubility determination, so the encountered solubility values do not correspond to the initial forms of the compounds, but to the hydrated compounds.
On the other hand, adefovir dipivoxyl, an antiviral drug, has been formulated with resorcinol, orcinol and hydroquinone as coformers. They show improved dissolution profiles with respect to the single solid form, particularly the cocrystals of orcinol and resorcinol. Moreover, dynamic dissolution experiments that simultaneously mimic both the pH variation along the gastrointestinal tract and the partition into biological membranes show that, in addition to the faster initial dissolution, adefovir dipivoxyl also penetrates faster into the organic membranes when formulated as resorcinol or orcinol cocrystal.