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Host-guest chemistry of antibacterial molecular crystal in supercritical CO_2 with solvent

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Abstract (less than 300 words)

There are several techniques to improve the properties of a medicine, such as polymorphs of crystals, amorphization, salts, and co-crystals [1]. In particular, host-guest chemistry, which means fixing CO_2 molecular inside of drug molecular crystal, is expected to enhance drug solubility and improve drug dissolve behavior, because released CO_2 in water can lower pH locally. In addition, this technique would achieve the advantages of easy handling, safety in terms of less harmful solvents, and high yields compared to the other methods.

In this work, we focus on the mechanism of host-guest chemistry for drug molecular crystal with CO_2 by conducting both experimental and computational approaches on "how much the host-guest chemistry accelerated by a cosolvent in supercritical CO_2".

We choose Enoxacin as target medicine, which has low solubility (< 0.1 mg/ml in water at 25℃)[2]. For the experiment, Enoxacin was placed in a container and contacted with $scCO_2$ at 80℃ and 20 MPa for 2 h in the presence of some solvents (EtOH, 1-PrOH, 1-BtOH, Acetone, Ethyl acetate). As a result, the solvents with hydroxy groups accelerates host-guest chemistry, which means Enoxacin can capture more CO_2 inside of its crystal. For the computational calculation, using quantum chemistry and thermodynamic calculations, we constructed a model to describe the host-guest chemistry for drug molecular crystal with CO_2, which has 2 steps: (1) relaxation of crystal structure pairing with CO_2, (2) recrystallization while retaining CO_2 inside. As a result, the experimental result is well explained by enthalpy change in the process (1) in the model. That is the solid dissolution of $scCO_2$ at the interface is an important process on the formation of host-guest drug molecular crystal with CO_2.

References

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