Probing Nonlinear Optical (NLO) Microspectroscopy for Heterogeneous Crystallization Development

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Crystallization offers a cost-effective and convenient way to purify and isolate active pharmaceutical (API) molecules in a reproducible manner [1, 2]. A better understanding of the crystallization process is essential considering process control and productivity. In this work, a tactical approach to control the crystallization of active pharmaceutical ingredients by gel-induced crystallization and heterogeneous surfaces has been applied to four model drug molecules. It is observed that nucleation events and crystal growth are guided by molecular recognition at interfaces through different weak intermolecular interactions.

To determine how the heterogeneous interactions influence the kinetics of the crystallization process, the nucleation and particle growth inside the organogel and heterogeneous surface are examined by in-situ non-linear optical microscopy (NLO) [3]. Wide-field second-harmonic generation (SHG) offers an opportunity to sensitively probe the crystallization inside gels and on surfaces with a high temporal resolution while scanning SHG microscopy enables 3D visualization of crystallization inside gels.

[1] Bora et al. Oriented crystallization on organic monolayers to control concomitant polymorphism. Chem. – A Eur. J. 2020; 26:699-710.
[2] Saikia et al. Drug mimetic organogelators for the control of concomitant crystallization of barbital and thalidomide. Cryst. Growth Des. 2020; 20 (12):7989-7996.
[3] Ahmet RD. et al. Nonlinear optical probes of nucleation and crystal growth: recent progress and future prospects. J. Mater. Chem. C, 2021; 9:11553-11568.