MS37-05 | Understanding the Role of Molecular Mobility in Phase Transitions of Bulk and Confined Pharmaceuticals

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Understanding the phase transitions of pharmaceuticals is of increasing importance from both academic and industrial perspective. This is because different polymorphs of the same drug have different intrinsic properties such as compressibility or dissolution rate. The combined analysis of structure and dynamics of bulk and confined pharmaceuticals, as well as understanding the role of molecular mobility in polymorphic phase transitions present a considerable challenge. Solid-state NMR spectroscopy is well placed to probe both structure and dynamics of the molecules as bulk and confined nanocrystals due to its sensitivity to intermolecular interactions at different length scales from Å to mm and dynamic regimes from 10^{-10} to 10 s.

This project aims at understanding the role of molecular mobility in phase transitions of bulk and confined pharmaceuticals using highly flexible, model drug with complex polymorphism (tolbutamide, TB) and variable temperature solid-state NMR analyses coupled with computational methods. TB form I as bulk and in the form of encapsulated nanocrystals inside the pores of MCM-41 mesoporous silica host were analyzed using solid-state NMR spectroscopy and relaxation measurements (^{1}H T_1, ^{1}H $T_{1\rho}$ and ^{13}C $T_{1\rho}$) under MAS conditions. The mobility is compared between bulk and confined drugs displaying coexistence of crystalline and amorphous species within the pores. Furthermore, significant differences in the dynamics of TB forms I^{L} and I^{H}, which differ only in the conformation of aliphatic tail are explained using a combination of solid-state NMR and MD simulations.