MS05-P10

Towards understanding phase transitions of confined pharmaceuticals

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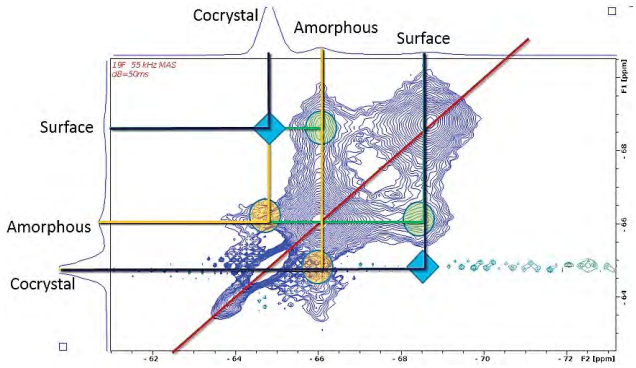
The change in the phases of matter has been extensively studied; from simplistic thermal changes of liquids, solids and gases to more the complex transitions of the different forms of the same material. This is important for pharmaceuticals because different polymorphs of the same drug having different intrinsic properties such as solubility and bioavailability. In studying these systems it is difficult to isolate different phases of matter in the early stages of crystallisation, as when these transitional phases occur they have a limited lifetime. Therefore stopping/slowing microscale crystallisation in order to observe the early stages is the aim of this project. This is achieved by encapsulating the pharmaceutical into a host with confined nanoscale geometry, in this case a mesoporous silica host. This allows for an indirect route into understanding relationships between different phases and motilities of pharmaceutical materials. Melt loading methods were used to in order to encapsulate the cocrystal of flufenamic acid and nicotinamide (FFA/NA) within the pores. Confirmation of loading at different ratios inside the pore was completed using DSC, nitrogen desorption isotherms. Subsequent NMR analysis was completed by solid state NMR methods to investigate the ^{1}H, ^{13}C and ^{19}F environments by different correlation experiments under MAS conditions. Defined separate phase peaks using ^{19}F NMR were observed previously in this material; surface, crystalline and amorphous peaks. Using ^{19}F-^{19}F NOESY NMR, interactions between these peaks were observed giving two out of the possible three interactions giving insight into spatial differences between the different phases of material.



References:

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Novel fluorescent probes for retinoic acid binding proteins

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Development of new, fluorescent, retinoic acid analogues offers the opportunity to investigate retinoic acid binding proteins both in vitro and in vivo. Retinoic acid signaling is vital for normal growth and development, and offers an attractive target for novel therapies, particularly within the field of neurodegenerative disease. Through different binding affinities the capability of, and variation between, different protein isoforms can be investigated, and potentially harnessed to design isoform-specific ligands. The fluorescent nature of the probes, and their enhanced stability over that of retinoic acid, makes them ideal for following in vitro via fluorescence spectroscopy and will be invaluable for high throughput ligand screening - feeding into the structure based design of future ligands.

Keywords: Retinoids, Binding, Fluoresence