FA1-MS05-P08

Use of Simultaneous X-ray Diffraction and Differential Scanning Calorimetry. Paul Pennartz[c], Joseph D. Ferrara[a], Akira Kishi[b], *[a]Rigaku Americas Corporation, 9009 New Trails Drive, The Woodlands, TX, USA 77381. [b]Rigaku Corporation, 3-9-12 Matsubara-cho, Akishima-shi, Tokyo, Japan, 196-8666. [c]Rigaku European Headquarters, Gross-Berliner-Damm 151, 14167 Berlin, Germany.*
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Polymorphism is a known problem for many drugs and drug candidates. Bioavailibity often varies with the specific polymorph, directly affecting efficacy. Thus, it is important to understand the changes a drug or drug candidate might undergo during galenic formulation and downstream handling. We have developed a second generation differential scanning calorimetry (DSC) attachment that provides a basic variable temperature stage (RT to 350°C and optionally
-40°C to 350°C) with the ability to perform a complete DSC experiment. We have also developed the software tools that integrate the x-ray diffraction (XRD) and thermal analysis experiments into a single tool that can monitor phase changes and phases as function of temperature. With an additional humidity control device these experiments can be modified to show the effects of humidity. Using XRD-DSC we have studied numerous drug compounds, including cimetidine, theophylline and terfernadine, as well as the reaction between urea and succinimide. We will demonstrate the utility of XRD-DSC in the drug discovery process. An example of the information that can be learned from XRD-DSC method is shown in Figure 1. Here we see the various phase transitions of α,α-trehalose dihydrate, an excipient, as a function of temperature both structurally and thermodynamically.

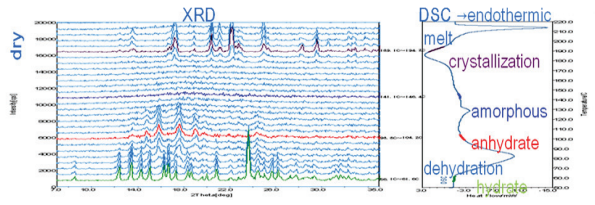

Figure 2. Phase changes and associated powder XRD as function temperature and heat load for α,α-trehalose dihydrate.

Keywords: Powder Diffraction, Phase Transition, Polymorphism

FA1-MS05-P09

Structural Aspect of Stabilization of Magnetic Particles in Solution: SAXS Study. Eleonora Shtykova[a], Petr Konarev[b], Lyudmila Bronstein[c], Dmitri Svergun[b]. *[a]Institute of Crystallography, Russian Academy of Sciences, Moscow, Russia. [b]EMBL Hamburg Outstation, Germany. [c]Indiana University, Department of Chemistry, USA.*
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A problem of stabilization of iron oxide magnetic nanoparticles (NPs) in solution is of special importance due to their possible application in life science, medicine, and particularly in anti-cancer therapy. Precondition for such applications is water solubility, which can be achieved by introducing a biocompatible shell on the hydrophobic NP surface. These coatings must fulfill certain requirements, and, first of all, they must prevent the aggregation of nanoparticles in solution. Functional properties of the protective shells depend strongly on their thickness, density, chemical composition and structure. Moreover, the practical use of the ferromagnetic liquids is determined by the metal particle shapes, size and size distributions. Therefore, all these characteristics of the specimens should be comprehensively characterized. In this work we report structure and properties of iron oxide NPs synthesized by decomposition of iron oleates and encapsulated by different methods. We analyze also the process of micellization of differently grafted PMAcOD in water solution, and the ability of the various coatings to encapsulate the NPs. The detailed structural investigation of the specimens was performed using small angle X-ray scattering (SAXS) and a complex of modern tools of SAXS data interpretation and modeling.

This work has been supported, in part, by the NATO Science for Peace Program (grant SfP-981438), NSF grant BES-0322767, MetaCyt funds and the grant of Leading Scientific School Program 1955.2008.2

Keywords: small-angle X-ray scattering, structure determination, computer modeling

FA1-MS05-P10

SAXS, CD and DLS Studies on Plant Heterotrimeric G protein Gamma subunit; AGG2. Anıl Aktürk, Burcu Kaplan-Türköz, Zehra Sayers. *Biological Sciences and Bioengineering,Sabanci University Istanbul, Turkey.*
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Heterotrimeric G proteins are mediators that transmit external signals arriving at receptor molecules to effector molecules and play a crucial role in signal transduction in mammalian and plant systems. The heterotrimer consists of alpha, beta and gamma subunit; alpha subunit has GTP binding and hydrolysis activity, whereas beta and gamma subunits are found as a dimer independent of heterotrimer state. The crystal structure model of mammalian betagamma dimer shows that the helical gamma subunit makes coiled-coil interactions with beta [1]. There is no individual structural model for mammalian gamma subunits; exceptionally no structural study exits for any plant heterotrimeric subunit.
We cloned and expressed Arabidopsis thaliana alpha (GPA1) using *Pichia pastoris* and beta (AGB1) and gamma (AGG1/2) subunits using *E. coli*. GPA1 was purified, characterized by SAXS, DLS and CD and shown to be active by GTP binding and hydrolysis assays. [2]. The beta and gamma subunits, AGB1 and AGG2 respectively, have been expressed in E. coli and the proteins have been purified for further studies including in vitro interaction of subunits [3].
We have carried out SAXS measurements on the gamma subunit, AGG2 and initial results indicate that the recombinant protein is present in the solution in different oligomeric forms. AGG2 tetramer was dissociated to dimer with increased DTT concentrations. Circular dichorism spectrapolarimety measurements show an increase in helical content and dynamic light scattering measurements show a decrease in hydrodynamic radius with increasing DTT concentrations. The structural model of AGG2 in solution and the effect of DTT