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.

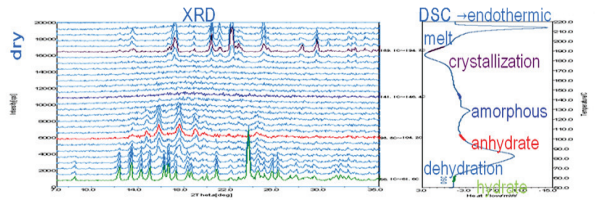

Figure 2. Phase changes and associated powder XRD as function temperature and heat load for α,α-trehalose dihydrate.

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

on protein size, secondary structure and overall conformation will be presented. The characterization of the solution structure and oligomerization state of the Arabidopsis gamma subunit is novel and important contribution to studies on G-proteins providing insights also for the mammalian proteins

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Keywords: GTP-binding proteins, biophysical analysis, SAXS

FA1-MS05-P11

Structural Analysis of 1-aryl-3-isopropilamino-1-propanone hydrochlorides. Barış Anıl[a], Ertan Şahin[a], Ebru Mete[a], H. İnci Gül[b]. [a]*Department of Chemistry, Faculty of Science, Atatürk University; Erzurum 25240, Turkey*. [b]*Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Atatürk University; Erzurum 25240, Turkey.*
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Mannich bases are generally formed by the reaction between formaldehyde, a secondary amine and a compound containing reactive hydrogen atoms. They display varied biological activities such as antimicrobial [1], cytotoxic [2,3], anticancer [2], analgesic [4], anti-inflammatory [5] and anticonvulsant [6] and DNA topoisomerase I inhibiting activities [3].
In this study, it was planned to synthesize some Mannich bases having the chemical structure of 1-aryl-3-isopropilamino-1-propanone hydrochlorides, which are possible cytotoxic/ anticancer compounds. Aryl part was changed as C_6H_5, 4-$CH_3C_6H_4$, 4-ClC_6H_4, 4-BrC_6H_4, 4-HOC_6H_4. The logic behind the synthesis of the compounds was to investigate the effect of substituents having different electronic nature. The chemical structures of the compounds were determined by X-Ray diffraction, ^{1}H-NMR, ^{13}C-NMR, DEPT, gCOSY, gHMQC, GHMBC and double resonance techniques.

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Keywords: Mannich bases, X-Ray diffraction, chemical structure

FA1-MS05-P12

Experimental and DFT studies on a pyrimidine-thione derivative. Muharrem Dinçer[a], Namık Özdemir[a], İrfan Koca[b], İsmail Yıldırım[c]. [a]*Department of Physics, Faculty of Arts and Sciences, Ondokuz Mayıs University, 55139, Samsun, Turkey*. [b]*Department of Chemistry, Faculty of Arts and Sciences, Bozok University, 66200, Yozgat, Turkey*. [c]*Department of Chemistry, Faculty of Arts and Sciences, Erciyes University, 38039, Kayseri, Turkey.*
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In general, pyrimidines have found much interest for their widespread potential biological activities [1] and medicinal applications, thus their chemistry has been investigated extensively [2]. In particular, various analogues of pyrimidine-thiones possess effective antibacterial, antifungal, antiviral, anti-AIDS, insecticidal and miticidal activities [3].

FA1-MS05-P13

New developments in low power beam delivery systems with aspheric multilayer optics. Nicoleta Galatanu[a], Sergio Rodrigues[a], Ronan Mahé[a], Peter Hoghoj[a]. [a]*Xenocs SA, Sassenage, France.*
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Low power microfocus X-ray sources coupled to multilayer optics are increasingly used in single crystal applications benefiting from very low maintenance requirements and high brilliance x-ray beam. The performance of these systems is typically better than traditional high power rotating anode X-ray sources in particular for small crystal analysis. However the performance remains significantly lower compared to the new generation of microfocus rotating anode sources.
We will present new developments in the field of beam delivery systems made of low power sources providing increased beam brightness (photons per second per solid angle). We have indeed developed new aspheric multilayer optics with increased capture angle and focusing properties as well as a new source optic design for single crystal diffraction applications. Such new developments provide an increased intensity (photons per second per mm^2) of at least a factor two compared to previous generation of microfocus sealed tube systems.
With the collaboration of our academic partners, different crystals of various sizes have been studied with different sources optics combination and compared with rotating anode generators. We will illustrate the new developments impact for protein crystallography and single crystal diffraction applications.

Keywords: Single crystal diffraction, multilayer optics, laboratory sources

FA1-MS05-P14

SWAXS Studies on Topical Lamellar Liquid Crystal Drug Delivery Systems. Semra İde[a], Elif Hilal Soylu[b], Merve Aytekin[c], R. Neslihan Gürsoy[c], Süeda Hekimoğlu[c]. [a]*Hacettepe University, Faculty of Engineering, Department of Physics Engineering,06800 Beytepe-Ankara.* [b]*Karadeniz Technical University,*