S100B belongs to the highly conserved S100 family, a subclass of the EF-hand Ca^{2+}-binding proteins, constituted by 21 known members implicated in intracellular and extracellular regulatory activity[1]. It has been demonstrated that the binding of S100B and the C-terminal domain of p53, a well known tumor-suppressor protein, prevents p53 phosphorylation and tetramerization, blocking its anticancer activity [2]. This inhibitory activity has been related with S100B overexpression in some malignant tumors. This interaction between an anphypatic α-helix on a protein and a hydrophobic cleft on its partner is similar to other therapeutically relevant interactions suggesting the possibility to design small molecules inhibitors of protein-protein interaction. Few inhibitors have been identified so far by using a NMR-based screening [3,4]. Our objective is the identification of small molecules able to block the protein-protein interaction between S100B and p53, through the SAR by NMR approach, successfully developed and applied by Fesik and coworkers [5]. The biophysical screening was preceded from a computational screening aimed to filter fragments to be screened in the following assays. Siena Biotech's fragment collection was used for a virtual screening campaign based on docking and pharmacohore approaches, leading to the selection of 280 molecules. NMR-based screening (WaterLOGSY) was performed in order to identify interacting fragments and ^{15}N-HSQC analysis confirmed the interaction of the strongest binders. Co-crystallization trials have been set up for one of the most active molecules. Crystals of protein-ligand complexes grow in few days and the analysis of diffraction data provides good-quality electron density maps at about 1.9 Å resolution. The binding site of the fragment has been clearly identified and corresponds to p53 binding site, as it was previously determined by the above mentioned NMR experiments. Structure-based library design has started in order to increase the potency of the fragments, through fragment evolution. Crystallization trials to obtain binary complexes of S100B with all the identified fragments are still on going.

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Keywords: structure and function of protein; NMR spectroscopic investigations; X-ray structure determination

FA4-MS09-P09

Electronic Structure of $[RuCl_3(indazole)_2NO]$. Jozef Kožíšek[a], Marek Fronc[a], Marin Breza[a], Katharina Schiessl[b], Vladimir B. Arion[b]. [a]*Department of Physical Chemictry, Slovak Technical University, Radlinského 9, SK-812 37 Bratislava, Slovak Republic.* [b]*Institute of Inorganic Chemistry, University of Vienna, Währingerstr. 42, A-1090 Vienna, Austria.*
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The development of metallopharmaceuticals is a frontier area in bioinorganic chemistry where both the Ru(II) and Ru(III) coordination compounds play an important role [1]. We have synthesized a novel ruthenium nitrosyl compound, $[RuCl_3(indazole)_2NO]$ and studied its geometric and electronic structure.
An experimental data set (GEMINI R diffractometer, 100K, 47 runs, 147 740 diffractions, resolution 0.54Å) was measured. Data reduction was done by CrysAlis171.33.31 and an average redundancy of 12.8 gives R_{int} of 0.045.
After the multipole refinement the topological analysis was performed using XD package. Theoretical calculation was done using CRYSTAL06 and TOPOND software.
Comparison of experimental and theoretical results will be disscussed.
This work has been supported by Slovak Grant Agency APVV and VEGA (APVV-0093-07, SK-AT-0018-08 and 1/0817/08).

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Keywords: charge density; ruthenium; electronic structure

FA4-MS09-P10

Analysis of Organic Molecular Compounds and Pharmaceuticals from Their X-Ray Powder Diffraction Patterns. Pauline Martinetto[a], Michel Anne[a], Pierre Bordet[a], Julie Linol[b], Gérard Coquerel[b], Eric Dooryhée[a], Pierre Terech[c]. [a]*Institut Néel, CNRS-UJF, Grenoble, France.* [b]*IMR, Université de Rouen, Mont Saint Aignan, France.* [c]*INAC, CEA, Grenoble, France.*
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Pharmaceutical developers are more and more concerned by solid form of drugs because it dictates their properties, including stability, hygroscopicity, dissolution rate, solubility, and bioavaibility. These solids can be molecular crystals (often prepared as polycrystalline powders) or noncrystalline solids (less stable but often with desirable pharmaceuticals properties, such as faster dissolution rates). In the recent years, advances in methodology have enabled to characterize both solid forms using only X-ray powder diffraction data. We have already reported structural studies carried out on a special steroid derivative molecule (STNH) which exhibits spectacular properties of an efficient organogelator of saturated alkanes [1]. Here, the crystallographic behavior of different xerogel forms are now observed ex- and in-situ using laboratory and synchrotron X-ray powder diffraction together with conventional and global optimization methods. We also present the study carried out on the molecular compound (±) modafinil, known to crystallise in five pure polymorphic forms [2, 3]. Under high energy milling, a new phase is obtained, which is a defective phase likely related to the original forms I and III. We are currently studying the total scattering signal

by using the Pair Distribution Function analysis (PDF) together with structural Rietveld refinements to describe both the local structure and the long-range ordering.

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Keywords: powder crystallography; organic pharmaceutical structure determination; pair distribution function

FA4-MS09-P11

Crystal Forms of Trospium Chloride. Michal Hušák[a], Michaela Hájková[a], Jan Čejka[a], Michal Dušek[b], Bohumil Kratochvíl[a]. [a]*Department of Solid State Chemistry, Institute of Chemical Technology, Prague, Czech Republic.* [b]*Institute of Physics, Academy of Sciences, Prague, Czech Republic.*
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Trospium chloride is a antispasmodic drug used to treat overactive bladder and symptoms of urinary incontinence, frequency, and urgency. The active substance is produced by crystallization from ethanol and declared as anhydrate. We tried to crystallize trospium chloride from several solvents with the main target – to determine the crystal structure used in production.
The structure of anhydrate was preliminary solved from synchrotron powder diffraction data (group $P2_1$, Z =2) by SA methods in DASH software and refined in Accelrys Reflex. Single crystals of anhydrite were obtained from ethanol. The structure of the single crystal at 150K has symmetry $P2_1/c$. Due to disorder the molecule is reflected by a pseudo-symmetry mirror plane x -y+1/2 z with the ratio between the two variants 4:1. The same disorder exists in powder data at room temperature but here the structure is non- centrosymmetric ($P2_1$), the c parameters is half and the ratio between the variants is approximately 1:1. The difference is probably caused by a phase transition (to be confirmed). The disordered structures were refined by Jana2006 using rigid body approach. The possibility of multiphase or twinned structure was tested and excluded
During the next crystallization experiments we had prepared single crystals of methanol and acetone solvates. Their structures were refined in $P2_1/c$, Z=4.
A comparison of all four known trospium chloride crystal forms is given.
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Keywords: trospium chloride; antispasmodic drug; solvates

FA4-MS09-P12

Hydrogen Bonding in Spirohydantoin Compounds. Shivachev Boris[a], Nikolova Rositsa[a]. [a]*Central Labolatory for Mineralogy and Crystallography, Bulgarian Academy of Science, Sofia, Bulgaria.*
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In order to fully explore structure activity relationships (SAR) around spirohydantoin scaffold, we have characterized structurally and biologically a variety of oxygen (O-1, O-2) and nitrogen N-3 substituents of the hydantoin moiety and varied the size of the cyckloalkane ring. We initially examined SAR around N-3 of the hydantoin core. We also attempted to improve the potency by thio substitution of carbonyl oxygen. The variation of SAR resulting from modification of the cycloalkane ring was also investigated. Incorporation of functional groups at N3, O1and O2 positions of the hydantoin ring resulted in complete turnaround of anti-convulsant activity. The SAR variation associated with cycloalkane ring modifications proved to be very flat, showing little improvement. As hydantoin ring structural parameters remain practically unchanged in all structures the SAR suggests that subtle changes in hydrogen bonding are responsible for the observed thorough changes of biological activity. This contribution will present a comparative study of hydrogen bonding patterns in the studied hydantoin compounds.

Keywords: hydrogen bonds in organic crystals; structure-activity relationships of drugs

FA4-MS09-P13

Pair Distribution Studies on Three Polymorphs of Paracetamol. C.A. Reiss[a], M. Gateshki[a]. [a]*PANalytical B.V., Lelyweg 1, 7602 EA Almelo, The Netherlands.*
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Recently the third polymorph of paracetamol was described [1]. Unit cell parameters and spacegroup were determined, but the crystal structure is not solved yet. It seems that some kind of disorder is present which makes it impossible to determine the structure up to now. In this study a different approach is taken to determine the structure of this third polymorph of paracetamol.
The total scattering pair distribution function (PDF) analysis is used to analyze structures on a local scale. This function looks at the absolute value of the distance between the nearest neighbours, the next nearest neighbours and so on. In the molecule of paracetamol the distances between the individual atoms are known giving the possibility to detect in the PDF of the polymorphs the differences of intermolecular interactions and disorder.
In this study the PDF's of the three polymorphs of paracetamol will be discussed and an attempted will be made to determine the structure of polymorph III.
The data is collected using a standard laboratory system with an X-ray tube with silver anode.

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Keywords: polymorph; disorder; pair distribution function