FA4-MS10-O1

Towards Knowledge - Based Design of Pharmaceutical Crystal Forms. Peter A. Wood. *Cambridge Crystallographic Data Centre, Cambridge, UK.*
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The technique of co-crystallisation as a means to produce a solid dosage form of an active pharmaceutical ingredient (API) has been gaining popularity within the pharmaceutical industry. Co-crystals have the potential for greater flexibility and diversity in the created forms than salts or hydrates due to their compatibility with non-ionisable APIs and the large range of pharmaceutically acceptable coformers that are potentially available. The effective use of co-crystallisation for this purpose is clearly affected by the capacity with which the solid forms produced can be controlled and predicted.
The structural knowledge stored within the Cambridge Structural Database (CSD, [1]) is highly relevant to all aspects of crystal engineering and the understanding of intermolecular interactions at a fundamental level. The study of appropriate structural data is of prime importance when investigating these areas.
Recent software advances [2] have broadened the opportunities for using the CSD for design and control of crystal forms. This study focuses on the analysis of a large family of pharmaceutical co-crystals containing a consistent API component [3] to provide insight into intermolecular interactions in general as well as co-crystal design in particular.

[1] Allen, F. H. A; *Acta Cryst. B*, **2002**, 58, 380-388. [2] Macrae, C. F.; Bruno, I. J.; Chisholm, J. A.; Edgington, P. R.; McCabe, P.; Pidcock, E.; Rodriguez-Monge, L.; Taylor, R.; van de Streek, J.; Wood, P. A.; *J. Appl. Cryst.*, **2008**, 41, 466-470. [3] Childs, S. L.; Wood, P. A.; Rodriguez-Hornedo, N.; Reddy, L. S.; Hardcastle, K. I.; *Cryst. Growth Des.*, **2009**, 9, 1869-1888.

Keywords: knowledge-based design; packing analysis; crystal form

FA4-MS10-O2

Chemical Semantic Web Concepts, Ontology, Software, Database for 2D and 3D Structures from Resources such as the Protein Data Bank, PubChem and HIVSDB. Talapady N. Bhat[a], Anh-Dao Nguyen[a], Glen Noble[b], L. Cooney[b], Mohamed Nasr[c], Alex Wlodawer[d], Kalyan Das[d], Edy Arnold[d]. *[a]Biochemical Science Division, NIST, Gaithersburg, MD 20899, USA. [b]Cygnus Corporation, Inc, Rockville, MD 20852, USA. [c]NIAID, Bethesda, MD 20892, USA. [d] NCI/FCRDC, Frederick, MD 21702, USA. [e]CABM/ Rutgers University, 679 Hoes Lane, Picataway, NJ 08854, USA.*
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The HIV structural databases (HIVSDB, http://bioinfo.nist.gov/SemanticWeb_pr2d/chemblast.do, http://chemdb2.niaid.nih.gov) distribute one of the largest comprehensive collections of structural, biological and pre-clinical data on inhibitors, drug leads and clinical drugs for AIDS. These databases contain info on several thousand biologically active compounds from all classes (HIV PR, RT, CCR5, Integrase) of FDA approved drugs. Efficient and yet user friendly data management systems that support state-of-the-art annotation, visualization and query capabilities are crucial for the effective use of data for fragment based structural pharmacology and rational drug design. Semantic Web is the vision of the World Wide Web Consortium for enabling seamless integration of electronic data for data mining and knowledge generation across the Web. Robust and functionally relevant ontology plays a critical role in developing the data elements for a Semantic Web. Presentation will illustrate how Semantic Web concepts are used for novel annotation, data integration, storage, and query to manage and display structural (fragments, 2-D images and text-based) biological, and pre-clinical data. One of these techniques (Chem-BLAST[1]) developed allows rapid comparison of structural fragments using the Semantics commonly used in drug discovery process. At present majority of the data in HIVSDB are obtained by us by weaning through publications. Recently we have extended (http://xpdb.nist.gov/pdb/chemblast.html) the Chem-BLAST technology to cover all the ligands held in the PDB. This new effort provides a versatile ligand gateway for data available in the PDB. Another structural database that includes thermodynamics data for Biofuels (http://bioinfo.nist.gov/biofuels) will also be presented.

[1] Prasanna, M.D., et al., *Chemical compound navigator: a web-based chem-BLAST, chemical taxonomy-based search engine for browsing compounds.* Proteins, 2006. **63**(4): p. 907-17.

Keywords: bioinformatics; AIDS inhibitors; structural database and drug design

FA4-MS10-O3

Identification of Crystalline Phases of Cements Using X-ray Microdiffraction Techniques. Dmitry Popov[a], Rainer Daehn[a], Daniel Grolimund[a], Philip Pattison[b], Erich Wieland[a]. *[a]Paul Scherrer Institut, 5232 Villigen PSI, Switzerland. [b]European Synchrotron Radiation Facility, Swiss-Norwegian beamline, Grenoble France.*
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Micro X-ray diffraction (microXRD) is a powerful tool to investigate spatially resolved micro-scale heterogeneous systems. The aim of the present study was to develop microXRD data collection and reduction techniques to study heterogeneous materials with typical features on the micro-meter scale. MicroXRD was exemplarily applied to cementitious materials to gain structural information from selected micron-sized crystals within the whole matrix. Case studies and test measurements performed at the SLS microXAS and ESRF Swiss-Norwegian beamlines showed the feasibility of this task: major crystalline components of selected area of the samples and selected microcrystals

within the cement matrix could be reliably identified using powder diffraction and structural data bases. The search-match procedure was based only on experimental diffraction data from selected areas or selected crystals of the samples and qualitative information about their chemical composition. No other knowledge about mineral composition of the samples was required. The results were substantiated by crystal structure refinement against collected in situ intensity data. Some software issues and developments for routine operation will be presented. The future application of the developments is to identify newly formed mineral species in the chemically disturbed zone at the cement-Opalinus clay interface with micro-scale resolution.

Keywords: identification; cements; microdiffraction

FA4-MS10-O4

Biphenyls in Crystals: Conformations and Intermolecular Contacts. Olga V. Grineva. *Moscow M.V. Lomonosov State University, Chemistry Department, Moscow, Russia.*
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It is known that dihedral angle between phenyl planes in biphenyl molecule (φ) in gas phase is about 45° while in three solid phases it does not exceed 10°. There are several papers with statistical data concerning this parameter in substituted biphenyls (e. g. [1-3]) however they do not illuminate connections between preferential conformations of molecules and types of substituents or intermolecular contacts.
In this work, a comprehensive analysis of crystals containing biphenyls with small substituents (namely halogen atoms, OH, COOH, NH_2, NO_2, CN, CH_3, CF_3 and similar groups) was made on the basis of the Cambridge Structural Database. Structures with some other biphenyls were considered for comparison. Values of φ were investigated in relation to types and number of substituents, their positions, intermolecular contacts and supramolecular motifs.
For example, it was found [4] that as one could expect a fraction of planar and almost planar molecules (φ was in the interval from 0 to 5°) was higher (37 %) for 4,4'-biphenyls with small substituents than for biphenyls with arbitrary substituents in the 3,3',4,4',5,5'-positions (26 %) but besides this fraction was considerably higher for 4,4'-biphenyls having at least one OH-group (48 %). Specific intermolecular contacts (hydrogen bonds, halogen...halogen contacts and others) often lead to formation of infinite molecular chains or their fragments (trimers, dimers) in the crystals with 4,4'-biphenyls, connecting chemically different molecules in heteromolecular crystals.
It was revealed that position of a peak in φ distribution for biphenyls with one small ortho-substituent was almost the same (50°) as for biphenyls with one arbitrary ortho-substituent [3] though the range of the angle was narrower (from 38 to 70°). In case of biphenyls with four small ortho-substituents the angle changed from 70 (mainly from 80) to 90° with a peak at 85° except the biphenyls with four ortho-fluorine atoms having φ between 50 and 61°.

[1] Brock C.P.; Minton R.P., *J. Am. Chem. Soc.*, **1989**, 111, 4586. [2] Bis J.A.; Vishweshwar P.; Middleton R.A.; Zaworotko M.J., *Cryst. Growth Des.*, **2006**, 6, 1048. [3] Brameld K.A.; Kuhn B.; Reuter D.C.; Stahl M., *J. Chem. Inf. Model.*, **2008**, 48, 1. [4] Grineva O.V., *J. Struct. Chem.*, 2009, 50(4).

Keywords: conformational analysis; Cambridge structural database; intermolecular interactions and packing in small-molecule crystals