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X-ray non-ambient powder diffraction of paracetamol polymorph form III

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For a quarter of a century the isolation of polymorph from III of paracetamol has been a problem due to its instability. In 1997 P. Di Martino et al [1] published the first route to prepare form III of paracetamol but they were not able to observe an x-ray diffractogram from form III. Recently J.B. Burley et al [2] isolated the polymorphic form III, but they could not draw conclusions from the powder diffractogram due to the large non- crystalline fraction. In this paper we present x-ray powder diffraction data from paracetamol form III as well as data from forms II and I. Also data collected at non-ambient temperatures will be discussed. Lattice parameters and a structure for form III will be proposed on the basis of the collected x-ray powder diffraction data.

[1] P. Di Martino et al, Journal of thermal analysis vol.48 (1997) 447-458
[2] J. C. Burley et al, European journal of pharmaceutical sciences 31 (2007) 271-276

Keywords: X-ray powder diffraction, polymorphism, non-ambient

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Crystal structure of sodium valproate - a hint in understanding the valproate physiological action?

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The first ever detailed studies [1, 2] of the solvate and polymorphic forms of sodium valproate, an active component of the anticonvulsant medicine Epilim, unraveled that this compound can exist in at least eight different solid forms. Detailed structural characterization of all forms proved difficult due to the pronounced affinity towards moisture and instability at ambient conditions. Repeated recrystallization from hot acetone solution afforded mixture of two forms [1], including colorless, block-shaped crystals of sufficient X-ray diffraction quality. X-ray crystallography identified this form as trisodium hydrogentetravalproate monohydrate, $Na_3(C_8H_{15}O_2)_3(C_8H_{16}O_2)H_2O$, a monohydrated 3:1 solvate of sodium valproate with valproic acid. Special feature of this compound is the bilayer structure composed of hydrophilic sodium-oxygen cluster wrapped with hydrophobic cover formed by the alkyl residues. The crystal structure shows that the ions are organized as rectangular, stable cluster columns and held together by numerous ionic and hydrogen bonds. The preference for clusterization can be considered an indication for presence of similar formations in the ion channels of the living cells during the intake of the medicine. These observations can serve as the basis of a new approach towards the understanding of the strong physiological action of valproate.

[1] G. Petrusevski, P. Naumov, G. Jovanovski, S.W. Ng, Inorg. Chem. Commun. 11 (2008) 81-84.
[2] G. Petrusevski, P. Naumov, G. Jovanovski, G. Bogoeva-Gaceva, S.W. Ng, submitted for publication.

Keywords: sodium valproate, clusters, physiological action

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Identification of novel fragment-based hits for *P. berghei* orotidine 5'-monophosphate decarboxylase

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Fragment-based screening by X-ray crystallography was used to screen the therapeutically relevant malaria target *Plasmodium berghei* orotidine 5'-monophosphate decarboxylase (Pb-OMPDC) against a library of small drug-like molecules (fragments). The 600-membered compound library was assembled from internal as well as commercially available sources. Automated processes were utilized throughout for data collection and analyses including 'FedEx crystallography' with the Industrial Macromolecular Crystallography Association Collaborative Assess Team (IMCA-CAT) high brilliance synchrotron beamline, a crystal handling robotic system, and automated data processing and electron density map generation scripts. The fragment-based screening effort led to the identification of novel scaffolds for this target.

Keywords: X-ray Crystallography, fragment-based Screening, Drug Discovery

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SAXD/WAXD study on structural change of intercellular lipid matrix in skin by applying chemicals

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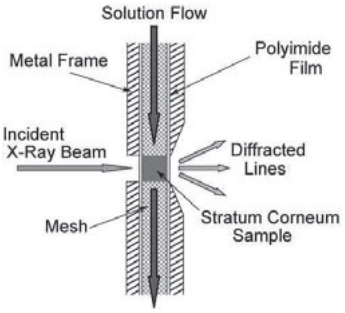
The evidence for the molecular-level structural change of the outermost layer of skin, stratum corneum, is highly desirable when the chemical agents such as cosmetics, drugs, etc. are applied. We propose a method to observe the minute structural changes in stratum coneum using a sample cell for SAXD/WAXD as shown in Fig. 1. By this technique the successive structural changes can be detected by tracking the X-ray diffraction profiles after the

application of the chemical agents and furthermore the problem of the individual difference of stratum corneum might be overcome since not the degree but the behavior of the structural changes seems to be less affected by the individuals. The performance of the present method was demonstrated in the extraction process of lipids from stratum corneum, the deterioration of barrier properties and the penetration mechanism in stratum corneum by ethanol application and the effect of a penetration enhancer of d-limonene to stratum corneum. Based upon these studies, we can propose that in the study of function in stratum corneum this method enables the molecular-level evaluation of the effects of cosmetics, drugs, etc.



Keywords: lipids, SAXD/WAXD, stratum corneum

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XRPD lab instrument measurements and crystallographic analysis on insulin and insulin derivatives

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A successful first structure refinement of lysozyme [1] already proved the value of standard XRPD laboratory instruments for protein structure research. In this contribution we will present new measurements and crystallographic analysis results of insulin and insulin derivatives performed on data from a PANalytical X'Pert Pro diffractometer (equipped with a capillary spinner, a focusing mirror and an X'Celerator detector). We additionally demonstrate that even fast measurements on a 96 well plate as used for polymorph screening purposes, result in high quality data, which is suitable for automatic crystallographic analyses like indexing [2] and LeBail [3] fitting.
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[2] A.Boultif and D. Louër, Powder pattern indexing with the dichotomy method, J. Appl. Cryst. (2004), 37, 724 - 731.
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Keywords: X-ray diffractometry of polycrystal compounds, polymorphism, protein structure analysis

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Teaching crystallography on-line by the Bilbao Crystallographic Server

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The Bilbao Crystallographic Server (www.cryst.ehu.es) is a web site with crystallographic databases and programs [1]. It can be used free of charge from any computer with a web browser via Internet. The on-line accessible databases and variety of applications convert the server in an excellent web tool for studying and teaching basic and applied crystallography. The server is built on a core of databases and the different applications are classified in shells. The innermost one is formed by simple retrieval tools accessing data from International Tables for Crystallography, Vol. A (Space-group Symmetry), Vol. A1 (Symmetry Relations between Space Groups) and Vol. E (Subperiodic Groups). The next shells contain applications that are essential for problems involving group-subgroup relations between space groups or representation theory of space and point groups. There are a number of applications related to problems of solid-state physics, crystal chemistry and theoretical crystallography: structural phase transitions, pseudosymmetry search, infrared and Raman selection rules, phonon extinction rules, etc. The programs on the Bilbao Crystallographic server have user-friendly interfaces with an on-line help. Some applications are linked to visualization applets. One of the important advantages of the server is that the different programs can communicate with each other and in this way the Bilbao Crystallographic Server has turned into a web-interactive environment with the appropriate tools for teaching theoretical and material crystallography.
[1] M. I. Aroyo, J. M. Perez-Mato, C. Capillas, E. Kroumova, S. Ivantchev, G. Madariaga, A. Kirov & H. Wondratschek. Z. Kristallog. (2006), 221, 1, 15-27.

Keywords: Bilbao Crystallographic Server, computer-aided crystallographic teaching, web resources

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Cambridge Crystallographic Database System utilization in undergraduate chemistry teaching

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Many aspects of chemistry education, particularly when teaching undergraduate students, rely heavily upon 3-D molecular visualization. Currently there is widespread interest in e-learning and efforts to prepare computer based teaching materials for molecular visualization are ubiquitous. Most are based on theoretical structures, which is often sufficient. Nonetheless, with the Cambridge Structural Database (CSD) containing rapidly approaching 500,000 entries of crystallographically determined atomic coordinate for organic containing small molecules, there exists a vast resource for teaching molecular visualization as well as examining molecular bonding in general. The CSD and its associated programs, known as the Cambridge Crystallographic Database System (CSDS) are predominantly used as research tools. This poster explores some of the potential teaching uses of the CSDS. Through funding from the National Science Foundation Discovery Corps Fellowship (NSF-DCF) program, the author has been providing CSDS access