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

Céleste A. Reiss[1], Kees Goubitz[2]
[1]PANalytical B.V., Lelyweg 1, Almelo, Overijsel, 7602 EA, The Netherlands, [2]Laboratory for Crystallography,Universiteit van Amsterdam, Valckenierstraat 65, Amsterdam,1018XE, The Netherlands, E-mail：Celeste.Reiss@PANalytical.com

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?

Gjorgi Petrusevski[1], Pance Naumov[1,2], Gligor Jovanovski[1,3], Seik W. Ng[4]
[1]SS. Cyril and Methodius University, Faculty of Science, Institute of Chemistry, P.O. Box 162, Arhimedova 5, MK-1001, Skopje, Macedonia, [2]Graduate School of Engineering, Osaka University, 2-1 Yamadaoka, Suita 565-0871, Osaka, Japan, [3]Macedonian Academy of Sciences and Arts, P.O. Box 428, MK-1001 Skopje, Macedonia, [4]Department of Chemistry, University of Malaya, 50603 Kuala Lumpur, Malaysia, E-mail：gjorgi_petrushevski@yahoo.com

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

Nicholas Chirgadze[1,2], Robert Lam[1], Kevin Battaile[3,4], Roni Gordon[1], Gera Kisselman[1], Jennifer Artz[5], Raymond Hui[5], Lisa Keefe[3,4], Cheryl Arrowsmith[1,5], Emil Pai[1,6]
[1]Ontario Cancer Institute, 200 Elizabeth Street, MBRC 5R406, Toronto, ON, M5G 2C4, Canada, [2]Department of Pharmacology and Toxicology, University of Toronto, Toronto, Ontario M5G 2C4, Canada, [3]IMCA-CAT, Argonne National Lab, Argonne, IL 60439, USA, [4]Consortium for Advanced Radiation Sources, University of Chicago, Chicago, IL 60439, USA, [5]Structural Genomics Consortium, Toronto, Ontario M5G 1L5, Canada, [6]Department of Biochemistry, University of Toronto, Toronto, Ontario M5G 2C4, Canada, E-mail：nickolay.chirgadze@uhnresearch.ca

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

Ichiro Hatta[1], Hiromitsu Nakazawa[2], Yasuko Obata[3], Noboru Ohta[1], Katsuaki Inoue[1], Naoto Yagi[1]
[1]Japan Synchrotron Radiation Research Institute, Industrial Application Division, SPring-8 1-1-1 Kouto, Sayo, Hyogo, 679-5198, Japan, [2]Kwansei Gakuin University, 2-1 Gakuen, Sanda, Hyogo 669-1337, Japan, [3]Hoshi University, 2-4-41 Ebara, Shinagawa, Tokyo 142-8501, Japan, E-mail：hatta@spring8.or.jp

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