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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,  $\text{Na}_3(\text{C}_8\text{H}_{15}\text{O}_2)_3(\text{C}_8\text{H}_{16}\text{O}_2)\text{H}_2\text{O}$ , 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 corneum 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