

MS53.P15*Acta Cryst.* (2011) **A67**, C564**Low-temperature polymorphic transitions in chlorpropamide and tolbutamide**

Tatiana N. Drebuschchak, Elena V. Boldyreva, *Institute of Solid State Chemistry and Mechanochemistry SB RAS, Novosibirsk, (Russia). REC-008 Novosibirsk State University, Novosibirsk, (Russia).* E-mail: tanya@xray.nsu.ru

Structure solution of molecular crystals at low temperatures does not necessarily mean, that it is the same as at ambient temperature, even if there are no visible changes in the crystal colour, shape, transparency and integrity on temperature variation. This can be illustrated at the examples of two recently discovered low-temperature polymorphic transitions in the antidiabetic drugs with related molecular structures, chlorpropamide, C₁₀H₁₃ClN₂O₃S, [1], and tolbutamide, C₁₂H₁₈N₂O₃S, [2]. These transitions are reversible and leave the crystals intact. Solving crystal structure at low temperature only, one cannot make a correct conclusion on the crystal structure under the crystallization conditions.

The polymorphic transitions are very interesting, since they are accompanied by a peculiar conformational ordering on cooling, resulting in an increase in *Z'*. In other words, several conformers not related by any symmetry operations are distributed regularly in the crystal structures of the low-temperature forms, in contrast to high-temperature phases, which have only one conformer per unit cell. An increase in *Z'* is accompanied by changes in either the elementary translations, or the crystal system. Thus, at temperatures below 260 K β-chlorpropamide transforms from the orthorhombic into the monoclinic polymorph, and this transition is accompanied by non-merohedral twinning; below 150 K one of the cell parameters doubles. In tolbutamide III below 150 K one of the cell parameters triples. All the transitions were studied by single-crystal and powder variable-temperature X-ray diffraction. The crystal structures of the high-temperature and low-temperature polymorphs were solved and refined at multiple temperatures. The changes in the translational symmetry was shown to be related to the regular changes in the conformations of the alkyl tails in some of the molecules, regularly distributed in the structure. All the low-temperature transitions were observed on cooling the polymorphs, which are metastable already at ambient conditions. At the same time, the stable forms of these compounds, which correspond to the commercially available samples, do not undergo any phase transitions on cooling.

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[1] T.N.Drebuschchak, V.A. Drebuschchak, E.V. Boldyreva, *Acta Cryst.* **2011**, *B67*, 163-176. [2] T.N.Drebuschchak, N.A. Pankrushina, E.V. Boldyreva, *Doklady Phys. Chem.* **2011**, *437*, 61-64.

Keywords: phase transitions in solids, drug polymorphism, low-temperature structure

MS53.P16*Acta Cryst.* (2011) **A67**, C564**Detection, by X-Ray Diffraction, of new bisphosphonate polymorphs of alendronate and risedronate treated hydroxyapatite**

Fernández, María Emilia,^a Fábregas, Ismael,^{b,a} *DEINSO-CITEDEF-CONICET (Dep. de Invest. en Sólidos- Centro de Invest. Científicas y Técnicas del Min. de Defensa - Comisión Nac. de Invest. Científicas y Técnicas) - Juan B. de La Salle 4397, Villa Martelli, Buenos Aires,*

CP: B1638ALO, Argentina- Te: 54 11 4709 8145, Fax: 54 11 709 3621. E-mail: mrapp@citedef.gob.ar

Introduction: We studied the physicochemical characteristics of the processes taking place on the surface of the bone of osteoporotic people treated with bisphosphonates.

In vitro essays were performed in osteoporotic human bones and in synthetic hydroxyapatite (Ha).

Alendronate and risedronate were used to treat bone samples and synthetic Ha. Both drugs are used almost exclusively in anti-resorptives therapies for bone diseases, and in post-operative treatments for cancer ablation (breast, prostate, etc.)

Methods: The nano hydroxyapatite was synthesized by the sol/gel method. The material obtained was analyzed by x-ray diffraction and Scherrer's equation to determine its crystallinity. The X-ray diffraction (diffractometer and radiation synchrotron) pattern of synthetic hydroxyapatite was compared with healthy human bone obtaining an excellent correspondence. The lattice parameters were determined by the Rietveld method. Scanning Electron Microscopy was used to obtain the Ca/P ratio and transmission electron microscopy to study the microstructure.

In Vitro treatment simulating the natural conditions in which the drugs interact with the patient's bones and synthetic hydroxyapatite (temperature and medium) was performed using alendronate and alendronate/risedronate respectively.

Results: None of the analysis methods used was able to match a known polymorph to that found on the surface of the bone. They were able to ascertain that its composition was the same, in all cases, to that of the known polymorph.

Conclusions: We observed a formation of new polymorphs in the treated surfaces; they have been characterized but not identified as any of those in the literature.

[1]- Kathryn L. Kavanagh, Kunde Guo, James E. Dunford, Xiaojie Wu, Stefan Knapp, Frank H. Ebetino, Michael J. Rogers, R. Graham G. Russell, and Udo Oppermann, **2005** The molecular mechanism of nitrogen-containing bisphosphonates as anti osteoporosis drugs. PNAS (Proceedings of the National Academy of Science of the United States of America) Canada. [2]- Ebetino, 1996 . Russell, 2007. Bisphosphonates mode of action and pharmacology. Pediatrics, 119 Suppl / 22007, S150-162. [3]- Delguste C., Lepaje O. M., Amory H., Doucet M. **2007** Pharmacologie clinique des bis phosphonates : revue de littérature axée sur le tiludronate chez le cheval. Ann. Méd. Vét., 151 269-280. [4]- James E. Dunford, Aaron A. Kwaasi, Michael J. Rogers, Bobby L. Barnett, Frank H. Ebetino, R. Graham G. Russell, Udo Oppermann, and Kathryn L. Kavanagh, **2008** Structure-Activity Relationships Among the Nitrogen Containing Bisphosphonates in Clinical use and Other Analogues: Time-Dependent Inhibition of Human Farnesyl Pyrophosphate Synthase J. Med. Chem., *51*, 2187:2195.

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MS53.P17*Acta Cryst.* (2011) **A67**, C564-C565**Novel polymorphs of curcumin**

Palash Sanphui, N. Rajesh Goud, U. B. R. Khandavilli and Ashwini Nangia, *School of Chemistry, Prof. C. R. Rao Road, University of Hyderabad, Hyderabad 500046, (India).* E-mail: sanphui.palash@gmail.com

Curcumin, a hydrophobic phenol (chemical name diferuloylmethane), is principal curcuminoid of the popular Indian spice turmeric, possesses diverse pharmacological effects including anti-inflammatory, antioxidant, antimalarial and anticancer activities.¹ It has negligible solubility (8.7µg/ml) in water, at acidic or neutral pH and also