Thematic Section: Research into New Technologies. **Full Paper**
Subsection: Structural Chemistry. *Reference Object Identifier* – ROI: jbc-01/17-51-8-105
The Digital Object Identifier – DOI: 10.37952/ROI-jbc-01/17-51-8-105
Submitted on August 20, 2017.

Stability of crystalline structure of paracetamol's molecular crystals generated by calorimetric scanning

© **Alexey P. Belyaev**,[1+] **Vladimir P. Rubets**,[2]* **Vladimir V. Antipov**,[2]* **Ekaterina Yu. Pavlova**
[1] *St.-Petersburg State Chemical Pharmaceutical Academy. 197376, St. Petersburg. Professor Popov St., 14. Letter A. Phone: +7 (812) 499-39-00. E-mail: rectorat.main@pharminnotech.com*
[2] *St.-Petersburg State Technological Institute (Technical University). Moscow Avenue, 26 Building 1 Letter A. St. Petersburg, 190013. Russia. Phone: +7 (812) 494-92-99. E-mail: office@technolog.edu.ru*

*Supervising author; +Corresponding author

Keywords*:* polymorphic transformations, structural studies, thermal studies, paracetamol.

Abstract

The results of investigation of the stability molecular crystal films of paracetamol with a rhombic modification are reported. The test samples were synthesized from paracetamol powder of monoclinic syngony by a special technique. The technique assumed vacuum evaporation, condensation, and subsequent calorimetric scanning. During the synthesis, a complex conversion of the crystals of the monoclinic syngony into a rhombic one took place. It was carried out by superposition of two phase transitions: a first-order transition with a density change and a second-order transition with a change in orderliness. The second-order transition proceeded as a blurred phase transition with the formation of some "pre-transition phase," witch irreversibly consumed in the process of phase transformation.

In the samples of molecular film of rhombic modification crystals of paracetamol the effect of temperature and mechanical action on the structure of molecular crystals was studying. The influence of temperature in a calorimetric cell and the influence of the mechanical effect inside a ball mill was explored. The studies included X-ray diffraction analysis, differential scanning calorimetry analysis and infrared spectroscopy. As a result of the research it was established that paracetamol films of molecular crystals of rhombic modification synthesized using calorimetric scanning have an increased sensitivity to temperature and mechanical action. It was found that the reason for the high sensitivity are the impurities of the crystals of the monoclinic modification remaining after the calorimetric scanning and promoting the polymorphic transformation of the crystals of the rhombic syngony into the monoclinic.

Data of X-ray phase analysis, infrared spectroscopy and differential scanning calorimetry are presented.

References

[1] H. Ahmed, M.R. Shimpi, S.P. Velaga. Relationship between mechanical properties and crystal structure in cocrystals and salt of paracetamol. *Drug Development and Industrial Pharmacy.* **2017**. Vol.43. No.1. P.89-87.
[2] F. Sun, B. Xu, Y. Zhang, S. Dai, X. Shi, Y. Qiao. Latent variable modeling to analyze the effects of process parameters on the dissolution of paracetamol tablet. *Bioengineered.* **2017**. Vol.8. No.1. P.61-70.
[3] Y. Boumrah, I. Bouzahia, S. Bouanani, K. Khimeche, A. Dahmani. Thermodynamic and analytical studies of drugs binary systems of paracetamol mixed with pseudoephedrine.HCl, dextropropoxyphene. HCl and tramadol.HCl. *Thermochimica Acta*. **2016**. Vol.634. No.6. P.48 56.
[4] J.M. Freitas, D.L.O. Ramos, R.M.F. Sousa, T.R.L.C. Paixão, M.H.P. Santana, R.A.A. Muñoz, E.M. Richter. A portable electrochemical method for cocaine quantification and rapid screening of common adulterants in seized samples. *Sensors and Actuators, B: Chemical.* **2017**. Vol.243. No.5. P.557-565.
[5] M. Taei, F. Hasanpour, M. Dinari, N. Sohrabi, M.S. Jamshidi. Synthesis of 5-[(2-hydroxynaphthalen-1-yl)diazenyl]isophthalic acid and its application to electrocatalytic oxidation and determination of adrenaline, paracetamol, and tryptophan. *Chinese Chemical Letters*. **2017**. Vol.28. No.2. P.240-247.
[6] A. Aliabadi, G.H. Rounaghi, M.H. Arbab. A new droplet-based polymeric banana electrochemical biosensor for analysis of one microliter solution of paracetamol. *Sensors and Actuators, B: Chemical.* **2017**. Vol.241. P.182-189.

[7] M.R. Carrasco-Díaz, E. Castillejos-López, A. Cerpa-Naranjo, M.L. Rojas-Cervantes. On the textural and crystalline properties of Fe-carbon xerogels. Application as Fenton-like catalysts in the oxidation of paracetamol by H_2O_2. *Microporous and Mesoporous Materials.* **2017**. Vol.237. No.1. P.282-293.
[8] L. Rimoldi, D. Meroni, E. Falletta, V. Pifferi, L. Falciola, G. Cappelletti, S. Ardizzone. Emerging pollutant mixture mineralization by TiO_2 photocatalysts. The role of the water medium. *Photochemical and Photobiological Sciences.* **2017**. Vol.16. P.60-66.
[9] C. Tan, N. Gao, J. Deng, L. Deng. Efficient degradation of paracetamol with nanoscaled magnetic $CoFe_2O_4$ and $MnFe_2O_4$ as a heterogeneous catalyst of peroxymonosulfate. *Separation and Purification Technology.* **2017**. No.3. Vol.175. P.47-57.
[10] V.G. Bessergenev, M.C. Mateus, I.M. Morgado, M. Hantusch, E. Burkel. Photocatalytic reactor, CVD technology of its preparation and water purification from pharmaceutical drugs and agricultural pesticides. *Chemical Engineering Journal.* **2017**. Vol.312. No.1. P.306-316.
[11] E. Szabados, G. Sági, F. Somodi, B. Maróti, D. Srankó, A. Tungler. Wet air oxidation of paracetamol over precious metal/Ti mesh monolith catalyst. *Journal of Industrial and Engineering Chemistry.* **2017**. Vol.46. No.2. P.364-372.
[12] P. Di Martino, P. Conflant, M. Drache, J.-P. Huvenne, A.-M. Guyot-Hermann. Preparation and physical characterization of forms h and hi of paracetamol. *Journal of Thermal Analysis.* **1997**. Vol.48. P.447-458.
[13] A.P. Belyaev, V.P. Rubets, V.V. Antipov, A.O. Ribnikov, S.A. Belyaeva. Crystallization of paracetamol of rhombic form. *Butlerov Communications.* **2014.** Vol.37. No.3. P.113-119. ROI: jbc-02/2014-37-3-113
[14] A.P. Belyaev, V.P. Rubets, V.V. Antipov, N.S. Bordei Formation of the molecular crystal structure during the vacuum sublimation of paracetamol. *Russian Journal of Physical Chemistry A*, **2015**. Vol.89. No.4. P.575-579. (russian)
[15] A.P. Belyaev, V.P. Rebets, V.V. Antipov, S.A. Belyaeva, A.V. Grishina. Vacuum condensation of filiform nanocrystals of cadmium sulfide. *Butlerov Communications.* **2016**. Vol.46. No.4. P.61-64. DOI: 10.37952/ROI-jbc-01/16-46-4-61
[16] A.P. Belyaev, V.P. Rubets, V.V. Antipov, S.A. Belyaeva. Crystallization of cadmium telluride on single crystal substrates cooled with liquid nitrogen. *Butlerov Communications.* **2015**. Vol.41. No.2. P.155-159. DOI: 10.37952/ROI-jbc-01/15-41-2-155
[17] A.P. Belyaev, V.P. Rubets, I.P. Kalinkin, M.Y. Nyzdin. Effects of ordering of an ensemble of disperse particles in a weak field of substrate elastic stresses during condensation from the vapor phase under sharply noneequilibrium conditions. *Russian Journal of Physical Chemistry A*. **2003**. Vol.77. No.10. P.16161-1665. (russian)