MS20 P07

Non-steroidal antiinflammatory drugs interaction with biological membrane Michal Markiewicz[a,b], Marta Pasenkiewicz-Gierula[b], Pawel Serda[c], Tadeusz Librowski[d], Szczepan Mogilski[d], Henryk Marona[e], Sergio Funari[f], Stanislaw Hodorowicz[a], [a]*Department of Crystal Chemistry and Crystal Physics, Jagiellonian University, Cracow, Poland,* [b] *Faculty of Biochemistry, Biophysics and Biotechnology, JU,* [c]*Regional Laboratory, JU,* [d]*Department of Pharmacodynamics, Medical College, JU,* [e] *Department of Chemical Technology of Drugs, MC, JU,* [f]*Max-Planck Institute for Colloids and Interfaces, c/o HASYLAB DESY, Hamburg, Germany.*
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Keywords: non-steroidal antiinflammatory drugs, molecular dynamics simulations, small and wide-angle diffraction

Non-steroidal antiinflammatory drugs (NSAID) belong to the most commonly used remedies. However, NSAID administration is often associated with several adverse effects, the most frequent being gastrointestinal complications, such as gastric ulcers and bleedings. The NSAID action relies on the cyclooxygenase (COX) inhibition, which leads to the prostaglandin synthesis suppression. The lack of prostaglandin's cytoprotective effect on gastric mucosa was previously thought to be fully responsible for their gastrointestinal toxicity. After the discovery of two subtypes of COX: COX1 and COX2, the former is considered physiologically active and responsible for the "gastroprotective" effect, while the latter is active during pathological processes. Unfortunately, gastrotoxicity of selective COX-2 inhibitors and non-toxic COX-1 selective inhibitors were also observed and suggested that there is additional mechanism of NSAID gastrotoxicity. Recently, that mechanism has been linked to direct NSAID's interactions with the gastric phospholipids [1]. These interactions may disturb the gastric mucosa hydrophobicity, which can result in lowered resistance of the gastric mucosa to luminal acid [2].
In this project, the influence of commonly used NSAIDs – aspirin, ketoprofen and piroxicam – with diverse gastrotoxicity and newly synthestized xanthone derivatives on the lipid bilayer structure and dynamics using both experimental and computer simulation approach was studied. The effects of NSAID with different toxicity on the bilayer thickness, lipid surface area, electron density profiles and other physical properties of the membrane were determined from molecular dynamics simulation giving opportunity to correlate the gastrointestinal side-effects with NSAID-membrane interactions at the atomic level. The multilamellar vesicles of POPC-cholesterol containing investigated NSAIDs were prepared and measured at different hydrations using SAXD and WAXD methods. The results of the measurements showed about 0.6nm diversity in the repeat periods *d* of the lamellar phase at 1:30 lipid-water molar ratio between aspirin and ketoprofen vesicles.

[1] Gummow R.J., Liles D.C., *Mat. Res. Bull*, 1993, 28, 1293.
[2] Grirrane, A.; Pastor, A.; Galindo, A.; Ienco, A.; Mealli, C. *Chemm. Commun.* 2003, 512.
[1] L. M. Lichtenberger, Z. Wang, J. J. Romero et al., *Nature Med* 1995, 1, 154.
[2] L. M. Lichtenberger, *Biochem Pharmacol* 2001, 61, 631.

MS20 P08

Negative Thermal Expansion in several solvated crystals form of an organic compound. J. Montejo-Bernardo & S. García-Granda, *Department of Physical and Analytical Chemistry, University of Oviedo. Asturias, Spain.* E-mail: jmmb@fq.uniovi.es

Keywords: Negative Thermal Expansion, X-ray analysis, TGA/DSC

The semi-synthetic compound azithromycin is mainly known by its high antibacterial capacity against both Gram-positive and Gram-negative bacteria. Recently, we have discovered a new and interesting property of (at least) some of its solvated crystalline forms. These crystals show Negative Thermal Expansion (NTE) in a wide range of temperatures, even above room temperature. This behavior is not usual for small organic compounds and, in the examples (only seven) found in the literature, except in one, the remaining studies were conducted at temperatures below room temperature.
In this work, we present the results of the thermal study by X-ray single crystal diffraction, X-ray powder diffraction, ThermoGravimetry (TG) and Differential Scanning Calorimetry of the crystalline solvated forms azithromycin + $2H_2O$; azithromycin + H_2O + ½ EtOH (or *i*-PrOH), and azithromycin + ½ H_2O + ½ EtOH (or *i*-PrOH). The DiHydrate form shows uniaxial NTE, while both MonoHydrate and SemiHydrate forms show biaxial NTE. As a consequence of this behavior, the increasing in unit cell volume is very small in all the cases (< 1%). Even, for the MH crystals it seems to decrease slightly within a specific range of temperature. Moreover, attending to thermogravimetric data, we can confirm that the shortening of the axes is not due to the loss of solvent molecules
This results demonstrate the great potential and versatility of these crystal forms of azithromycin in the field of soft chemical materials.

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Tricyclic systems as potential bio-scaffolds: testing their relative flexibility Paola Paoli, [a] Maria Altamura,[b] Paolo Dapporto,[a] Antonio Guidi,[b] Nicholas J. S. Harmat,[b] Loïc Jierry,[b] Patrizia Rossi,[a] *Department of Energy Engineering, University of Florence, Italy.* [b]*Chemistry Department, Menarini Ricerche S.p.A., Florence, Italy.*
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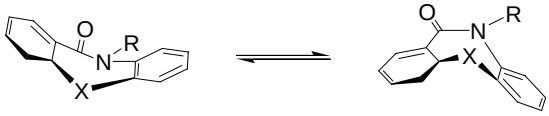
Keywords: ab-initio calculations, atropisomers, energy barriers

Tricyclic systems are amongst the most important scaffolds in medicinal chemistry and their possible inner chirality has been recognized for a long time. [1] 5-Ethyl-5,6-dihydro-11H-dibenzo[b,e]-6-one and the corresponding thiolactam are published examples of this



phenomenon.[2] We have considered these compounds on a scale of flexibility, at the rigid side of which, two kinetically stable atropisomers could appear. As a part of