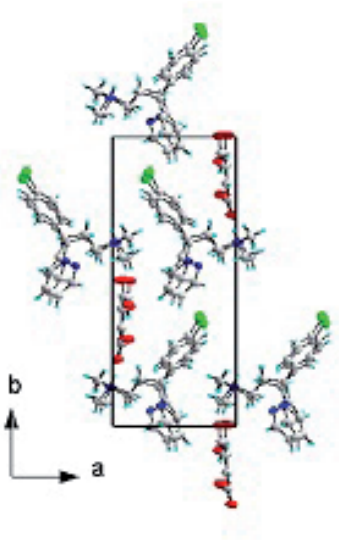
treat symptoms of allergic conditions such as rhinitis and urticara. In the Cambridge Structural Database (*CSD*) there is one report for the dextro isomer (REFCODE: CPHMAL10) and three reports in the Powder Diffraction File (PDF-4+: 00-041-1599, 00-042-1792, 00-050-2420). Similarly, there is one report in *CSD* and five in the PDF-4 for the racemic mixture. In an attempt to obtain polymorphic modifications of DexChlor, crystallization experiments were carried by slow evaporation and vapour diffusion using water, ethanol, methanol, acetone, dichloromethane and DMSO, among other solvents. The crystallization of DexChlor in acetone, by slow evaporation at 4-5 ºC, produced colourless prisms. The ***c*** parameter of the unit cell of this phase is twice the corresponding value for CPHMAL10. The asymmetric unit has two crystallographically independent molecules. The geometry of one of the molecules is such that it overlaps with the molecule obtained in the previous report but the second independent molecule has a different conformation. In the new dataset, the reflections with *l*=2n+1 are systematically weak but nevertheless present. Transformation of the atomic positions of CPHMAL10 and re-indexing of data in the smaller cell resulted in a non-satisfactory refinement of the structure. This indicated that the small cell does not represent correctly the structure of DexChlor. Thus, DexChlor crystallizes in the monoclinic system, space group $P2_1$ with unit cell parameters *a*=8.8872(6), *b*=20.3157(14), *c*=11.4666(7)Å, β=104.032(4)°, V=2008.5(2) $Å^3$, $Z=4$. A detailed description will be presented.



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Keywords: dexchlorpheniramine maleate, crystal structure, antihistaminic

MS53.P08

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Rapid Monitoring Polymorphism of Clopidogrel (Plavix)

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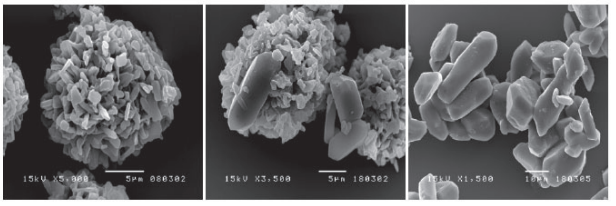
Polymorphic stability of drugs towards heat, moisture, oxidation and light is of great interest in pharmaceutical industry. Rapid monitoring of drug polymorphism in pharmaceutical processes by X-ray powder diffraction is a challenging task especially when the peaks of the different polymorphs overlapped [1]. Clopidogrel (PLAVIX) is a potent oral antiplatelet agent commercially and widely used in the treatment of diseases related to coronary artery, peripheral vascular and cerebrovascular.

Clopidogrel bisulfate (CPL^+ HSO_4^-) exists in many polymorphic forms (Form I to VII). Only Form I (monoclinic) and Form II (orthorhombic) are used in pharmaceutical formulation [2]. This work presents the rapid monitoring polymorphic change in the case of Clopidogrel and its formulations under various conditions of temperature, moisture and storage time under FDA regulations (Clopidogrel is given by Silom Medical Co. Ltd. Thailand).



0 day, Form I 1 month, Form I+II 3 months, Form II

[1] D. Giron *American Pharmaceutical Reviews* **2008,**. *11(1)*, 66-71, [2] *US patent No. 20070037842A1*, Polymorphs and amorphous form of (s)-(+)-clopidogrel bisulfate.

Keywords: rapid monitor, polymorph, pharmaceutical process

MS53.P09

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A Monoclinic Polymorph of the Ticlopidine Hydrochloride

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Antiplatelet therapy prevents ischemic events in patients with high risk of arterial-occlusive thrombosis and myocardial infarction. Ticlopidine hydrochloride (TICLID®) [1] is a platelet antiaggregating agent whose use as a potent antithrombotic pharmaceutical ingredient is widespread [2]. Only the crystal phase used for drug product manufacturing (form I) is known [3]. Here, a new polymorph of ticlopidine hydrochloride (form II) is discrebed for the first time.

A sample of raw ticlopidine hydrochloride powder was dissolved in MeOH by shaking the mixture at room temperature. This solution was allowed to stand in the dark for 5 days at 28 ºC within a crystal growth chamber. After this period, the solvent was completely evaporated and colorless prisms were grown on the bottom of the glass crystallizer. A clear crystal with dimensions of 0.55 x 0.09 x 0.07 mm was chosen for the single crystal X-ray diffraction experiment that was performed at room temperature using an Enraf-Nonius Kappa-CCD diffractometer. The X-ray beam was the graphite-monochromated MoKα line.

While the previous polymorph crystallizes in the triclinic space group *P-1* [3], the new crystal phase was solved in the monoclinic space group $P2_1/c$. Both polymorphs crystallize as racemic mixtures of enantiomeric $(ticlopidine)^+$ cations. Detailed geometrical and packing comparisons between the crystal structures of the two polymorphs have allowed us to understand how different supramolecular architectures are assembled. It was possible to conclude that the main difference between the two polymorphs is a rotation of about 120º on the bridging bond between the thienopyridine and *o*-chlorobenzyl moieties. The differential *o*-chlorobenzyl conformation alters the pattern of weak intermolecular contacts involving this moiety, leading to the change in crystal assembly and increasing the symmetry in the ticlopidine hydrochloride solid state form described for the first time in this study. Other conformational features are slightly different between the two polymorphs, as the thienopyridine puckerings and the *o*-chlorophenyl orientations. These conformational characteristics were also correlated to the crystal packing patterns.

The finding of a new polymorph of this important platelet

antiaggregating drug reveals that phase relationships should be investigated. Knowing the solid state properties of ticlopidine hydrochloride polymorphs would avoid unexpected bioavailability resulted from solubility and stability changes. Since ticlopidine hydrochloride is not well studied in terms of solid state structures and properties, this study means an advance in its characterization and understanding of conformational features and crystal packing patterns.
Acknowledgements: FAPEMIG (APQ-02685-09, APQ-01093-10), CAPES (AUXPE-PNPD 1865/2008), FINEP (Ref. 134/08), CNPq, PIBIC-UNIFAL-MG.

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Keywords: polymorphism, drug, pharmaceutical

MS53.P10

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Diversity of gossypol clathrates with pyrazine

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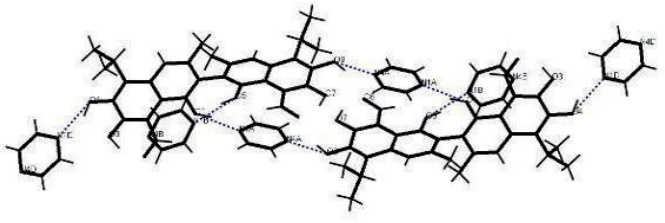
Gossypol, a yellow polyphenolic pigment of the cotton plant, has a wide range of biological action and is a surprisingly versatile host compound [1]. Single crystals of gossypol complex with pyrazine (1:4) have been obtained in the pyrazine solution of gossypol (t=56°C) and characterized by following crystallographic data: $C_{30}H_{30}O_8 \cdot 4(C_4H_4N_2)$, M=838.91, T=130 (2)K, MoK_a=0.71073Å, a=7.5230(3), b=13.9185(6), c=19.8328(8) Å, α=88.789(4), β=87.255(3), γ=86.683(4)°, V=2070.46(15) Å^3, Z=2, $D_{calc.}$=1.346 g/cm^3, crystal system triclinic, space group P-1. Pair of gossypol and pyrazine molecules are formed centrosymmetric tetramers untypical for gossypol type structures. Crystal structure is characterized with the presence of wide channels for guest molecules. Other gossypol inclusion complexes with pyrazine have been obtained from guest-free gossypol polymorphs P2, P3 and P4 by sorption of pyrazine vapors at room temperature and 50°C. When pyrazine vapors are absorbed at 50°C all three polymorphs of gossypol turn to one crystal form – a new clathrate of gossypol with pyrazine (1:4). Thus, when pyrazine vapors are absorbed at low temperatures, probably, formation of the new clathrate is limited on matrixes of corresponding polymorphs while at higher temperatures the crystal structure of polymorphs has a more tendency to form a clathrate.



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Keywords: clathrate, polymorphism, thermoanalysis

MS53.P11

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Formation of gossypol clathrates by vapor sorption

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Gossypol obtained from cotton seeds has valuable biological properties [1]. It is known that gossypol is a versatile host compound forming clathrates with any small molecule substances. The other specific feature of this compound is unusual polymorphism of gossypol's guest-free crystals [2]. We present here the results of gossypol clathrates decomposition and vapor sorption by its polymorphic apohosts. The clathrates considered are obtained with following five solvents - acetic acid (**I**), acetone (**II**), 1,4-dioxane(**III**), chloroform (**IV**) and benzene (**V**). Depending on the crystal structure guest molecules of studied clathrates are freed at different temperatures. TG-DSC curves show that H-clatrates are more stabile comparatively to that of gossypol clatrates. For the studied clatrates the stability decreases in the following order: **I→II→ IV → V → III**.

Gossypol polymorphs P2, P3 and P4 are obtained by desolvatation of clathrates. We have studied the formation of clathrates by gossypol polymorphs in result of vapor sorption. For this purpose vapors of easily sublimating naphthalene and benzoquinone are used. Sorption was performed at room temperature and at 50ºC. In both cases the sorption of naphthalene vapors by appropriate polymorphs shows some increasing in masses of initial polymorphs. On example of 3 polymorphs the mass increasing at room temperature was insignificant and inconsiderable on XRD-pattern but at 50ºC the essential sorption of naphthalene by all of 3 polymorphs has been observed. The formation of new phase was not observed by exposure of benzoquinone vapors on 3 gossypol polymorphs at temperatures given above.

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Keywords: clathrate, polymorphism, sorption

MS53.P12

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The crystal structures of gossypol reaction products with 4-aminoantipyrine

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Gossypol is a yellow pigment of cottonseed possessing antiviral, antitumor, anticancer, antifertile, immunosuppressive and other types of biological activity [1]. A chemical modification of its structure in many cases leads to low toxic derivatives. For this purpose the gossypol derivatives with 4-aminoantipyrine were obtained. Symmetrical bis-derivative of gossypol with 4-aminoantipyrine is named ragosin (**A**) and unsymmetrical mono-derivative – monoragosin (**B**). In this report the crystal structures of (**A**)/pyridine(**I**) (1:5) and (**A**)/(**B**)/ethylacetate (**II**) (1:2:5) will be discussed. Crystal data (**I**): triclinic, P-1, a=15.2331(10)Å, b=15.4459(10)Å, c=16.2360(15)Å, α=111.902(7)°, β=101.386(7)°, γ=91.788(5)°, V=3451.5(5)Å^3, Z=2, $D_{cal.}$=1.236 g/cm^3; (**II**): monoclinic, C2/c, a=20.5152(5)Å, b=25.6725(7)Å, c=30.9163(7)Å, β=92.558(2)°, V=16266.7(7) Å^3, Z=2, $D_{cal.}$=1.258 g/cm^3.

In the structure of (**I**), two ragosin molecules form dimers via the pair of centro symmetrical H-bonds O4-H…O3 (2.764 Å). Other three hydroxyl groups of ragosin molecule are involved in the formation of H-