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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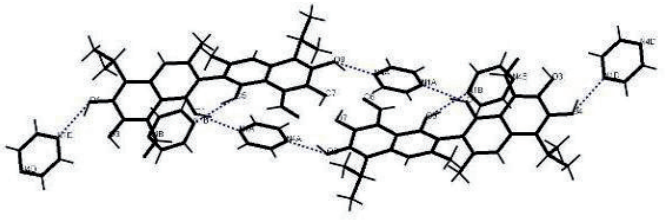
Gossypol, a yellow polyphenolic pigment of the cotton plant, has a wide range of biological action and is a surprisingly versatile host compound [1]. Single crystals of gossypol complex with pyrazine (1:4) have been obtained in the pyrazine solution of gossypol (t=56°C) and characterized by following 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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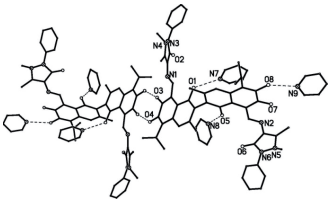
Gossypol is a yellow pigment of cottonseed possessing antiviral, antitumor, anticancer, antifertile, immunosuppressive and other types of biological activity [1]. A chemical modification of its structure in many cases leads to low toxic derivatives. For this purpose the gossypol derivatives with 4-aminoantipyrine 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.

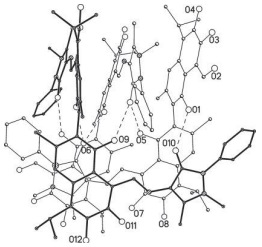
In the structure of (**I**), two ragosin molecules form dimers via the pair of centro symmetrical H-bonds O4-H…O3 (2.764 Å). Other three hydroxyl groups of ragosin molecule are involved in the formation of H-

bonds with pyridine molecules (O1-H…N (2.755 Å), O5-H…N(2.740 Å), O8-H….N(2.782 Å)). So, two ragosin and six pyridine molecules form associate. The other 2 guest molecules do not have H-bonding with **A** molecule and their position is stabilized only by Van-der-Waals and π-π (stacking) interactions.

The crystal structure of (**II**) is characterized by the presence of associates, consisting of two **B** molecules and one **A** molecule, formed by H-bonds of three types: with H-bonds O1-H...O10 and O9-H... O6 cross-linked molecule (**B**) with two molecules (**A**). In turn, two molecules of (**A**) are self associated by hydrogen bonds of the O5-H ...O6. It should also be noted that the molecule of **A**, and associate in general has a symmetry axis of the second order.



I



II

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Keywords: clathrate, supramolucular assembly, hydrogen bonding

MS53.P13

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Planarity and activity of aroyldithiocarbazoates

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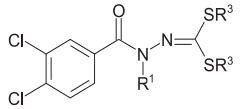
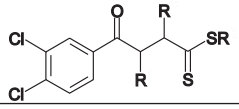
The increasing resistance of *Mycobacterium tuberculosis* to existing agents and the resulting spread of the pathogen, in both developed and developing countries, makes the search for new tuberculostatics an important issue.

The studied compounds were obtained by Foks and coworkers from Department of Organic Chemistry, Medical University of Gdansk as derivatives of aroyldithiocarbazonic acids (Scheme), showing tuberculostatic activity [1,2]. It was suggested that general planarity of the molecules could be prerequisite for activity [3] in this chemical class.

	Compound	R^1	R^2	R^3
	**1**	H		Me
	2	H		Bz
	3	Me		Me
	**4**	H	Me	Me
	5	H	Me	n-Bu

The planarity of molecules **1** and **2** is maintained by conjugations and intramolecular hydrogen contacts N-H…X(O,S). In structures **3**, **4** and **5** substitution of hydrogen at any N atom by a methyl group unables formation of those attractive interactions through N-H…O. As a result, the molecules **3**, **4** and **5** are not planar. In their crystals, molecules **1**, **4** and **5** form infinite chains C(4). Surprisingly, molecules **2** do not form any intermolecular hydrogen bonds (despite possessing unsubstituted amide group). Compound **1** showed the highest inhibition of *Mycobacterium tuberculosis* bacteria.

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[1] H. Foks, M. Janowiec. *Acta Pol. Pharm.* **1979,** *36*, 155-160. [2] H. Foks, C. Orlewska, M. Janowiec, *Acta Pol. Pharm. Drug Res.* **1992,** *49*, 47-50. [3] A. Olczak, M. Szczesio, J. Gołka, C. Orlewska, K. Gobis, H. Foks, M.L. Główka, *Acta Cryst.* **2011,** *C67,* o37–o42.

Keywords: tuberculostatics, planarity-activity relationship, aroyldithiocarbazoates

MS53.P14

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Polymorphism and co-crystal formation in the "glycine-carboxylic acid" systems

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SPolymorphism and co-crystal formation belong to "hot topics" in reactivity of organic solids. They are important for practical applications, in particular in pharmaceutical industry, because properties of different polymorphs differ, and the properties of co-crystals may also differ from those of a mixture of components.

Polymorphism is often related to the difference in hydrogen bond networks in the crystals. Crystallization of a desirable polymorph is known to be affected by pH. At the same time, pH is modified by adding acids, which can also act as co-crystal and/or salt co-formers. The aim of the present study was to compare the effect of a series of carboxylic acids on crystallization of glycine in a wide range of relative glycine : carboxylic acid concentrations. Crystallization from solutions was compared with the results of mechanochemical synthesis (co-grinding). The crystal structures of co-crystals were analyzed, with a special attention paid to the transfer of protons between amino acids and carboxylic acids in the solid state in relation to relative pKa values in solution. Examples of "true" co-crystals with no proton transfer between an amino acid and a carboxylic acid are given.

Depending on the carboxylic acid and relative glycine : carboxylic acid ratio the following results were obtained:

1. Recrystallization of glycine from alpha- to gamma- polymorph (at low concentration of most acids used), both in solution and in solid mixtures;

2. Formation of co-crystals and salts for some carboxylic acids (when the acid was added in a stoichiometric 1:1 ratio);

3. Crystallization of the two components in the mixture separately.

The results of the experiments are discussed in relation to the molecular structures of carboxylic acids, their pKa in solution, as well as relative solubility of glycine and a carboxylic acid in water.

The work was supported by grants from RFBR (09-03-00451; 11-03-00684), BRHE (RUX0-008-NO-06), by the Integration Projects No. 13 and 109 of the SB RAS, FASI Grants P2529 and 16.740.11.0166 and Projects 21.44 and 5.6.4 of RAS.

[1.] E.A. Losev, M.A. Mikhailenko, E.V. Boldyreva *Reports of Russian Academy of Sciences*. **2011**, submitted. [2] E.A. Losev, B.A. Zakharov, E.V. Boldyreva *Acta Cryst. C*, **2011**, submitted.

Keywords: crystallization, co-grinding, hydrogen bonds