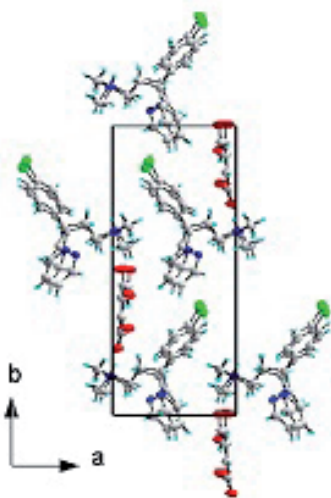


treat symptoms of allergic conditions such as rhinitis and urticaria. In the Cambridge Structural Database (CSD) there is one report for the dextro isomer (REFCODE: CPHMAL10) and three reports in the Powder Diffraction File (PDF-4+: 00-041-1599, 00-042-1792, 00-050-2420). Similarly, there is one report 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 °C, 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, $\beta=104.032(4)^\circ$, $V=2008.5(2)$ Å³, $Z=4$. A detailed description will be presented.



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Keywords: dexchlorpheniramine maleate, crystal structure, antihistaminic

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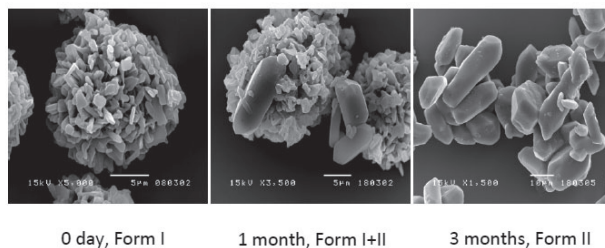
Rapid Monitoring Polymorphism of Clopidogrel (Plavix)

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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⁺ HSO₄⁻) 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).



[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

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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 described 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 °C 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 MoK α 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 120° 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