ESRF	**Experiment title:** Solution of crystal structure of Paclitaxel and low temperature form of Simvastatin from combined powder and solid state NMR data	**Experiment number**: CH-1845
Beamline: BM01B	**Date of experiment**: from: 17/11/2004 to: 18/11/2004	**Date of report**: 23.2.2004
Shifts: 3	**Local contact(s)**: Dr. Denis TESTEMALE	*Received at ESRF:*

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Report:

Paclitaxel

High resolution powder diffraction record of paclitaxel was recorded at 0.69956 Å wavelength and room temperature. 2 mm capillary was used to get maximal intensities. The only one reasonable cell was found by KOHL software (as part of CRYSFIRE): orthorhombic cell with following lattice parameters: a=28.094(2), b=33.513(3), c=9.6570(7) Å. All first 20 reflections were indexed with M_{20}=67.02 – Fig. 1.

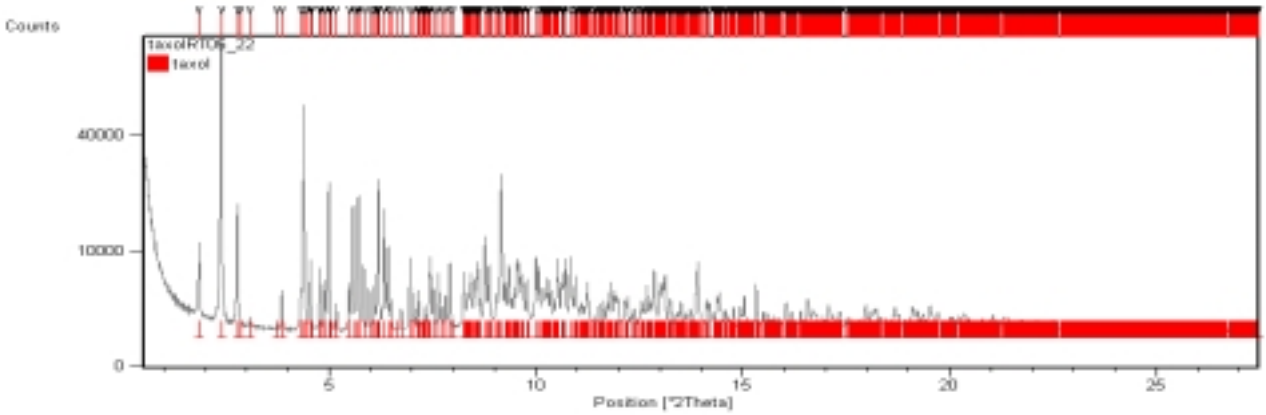

Fig.1 Powder diffraction record of paclitaxel with marked position of reflections predicted from indexation.

The missing reflections indicates $P2_12_12_1$ space group. The unit cell volume 9092.2 $Å^3$ corresponds to 2 independent paclitaxel molecules in the asymmetric unit cell. We were trying to solve the structure with program FOX, unfortunately the obtained solution was producing not-acceptable conformation of the

paclitaxel molecules. Just now we work on preparation of solid state NMR experiment with the following goals: to confirm the presence of 2 independent molecules in the unit cell, to obtain intermolecular restrains, to obtain inter-molecular restrains. The restrains will be later used as an input into the FOX system and we will try to solve the structure again.

Symvastatin

Measurement was done at 0.69956 wavelength. Sample was placed in 1.5 mm capillary. In the first step we had measured 12 fast scans during a slow sample cooling from 287 K to 150 K - fig 2.

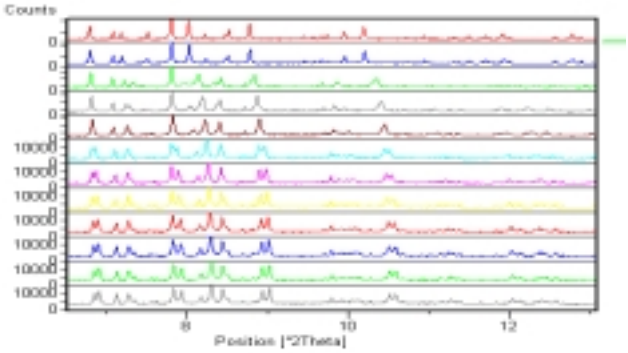

Fig.2 Changes of simvastatin powder diffractogram during continuous cooling from 287 K (top) to 150 K (bottom).

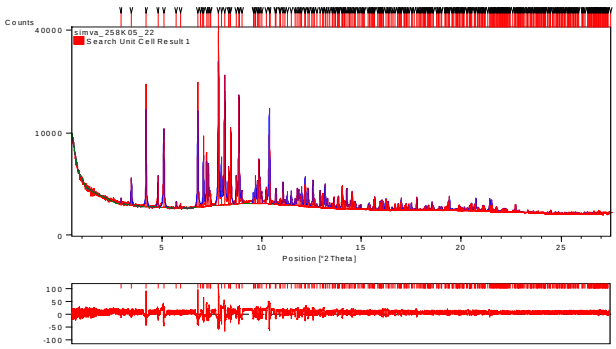

Fig. 3 result of Rietveld Refinemen – symvastatin phase II

The results confirmed the presence of 2 new simvastatin phases originally indicated by solid-state NMR. The phase I existing at room temperature transforms at approximately 260 K to phase II. In addition, phase II transforms to phase III at approximately 220 K. Phase III remains stable up to 150 K. During the data measurement it was visible, that the phase transformations are fully reversible. We had finally made 3 high-resolution measurements at 287 K, 258 K and at 200 K.

The data measured at 287 K corresponds to phase I (structure is already known from single crystal measurement) . Just to check the used methodology, we have successfully indexed this phase by DICVOL and solved the structure by the FOX software. The structure solution result corresponds to the single crystal data well. Lattice parameters: a=6.12275(8), b=17.3085(3), c=22.4566(4) Å space group $P2_12_12_1$.

The data of phase II measured at 258K were indexed by DICVOL: an orthorhombic cell with following lattice parameters: a=6.0874(2), b=16.7092 (6), c=23.1558(8) Å space group $P2_12_12_1$. The parameters of phase II are very similar to the phase I, but the changes in the peak intensities indicate more important structure changes than a simple unit cell contraction based on the temperature decrease. We have solved the structure of phase II by FOX software. Preliminary Rietveld refinement was done in Philips High Score Plus (Rp=11.5%, Rwp=16.6%) fig.3. The main difference in comparison to the phase I was found in the flexible ethyl terminal chains configurations. We will make much more precise comparison after restrained structure refinement in the GSAS system.

The data of phase III measured at 200K were indexed by DICVOL: a monoclinic cell with following lattice parameters: 6.0424(6), 16.282(1), 23.469(2) Å β=90.867(2)°. We expect, that the reason of the phase transition will consist in only a slight conformation change. The structure solution was not done up to now due to the unexpected icing of the capillary and the presence of the ice reflections in the pattern. We need to find a more sophisticated method how to remove ice diffraction contribution, or to measure the sample at the BM01B again using a better cooling system capable to avoid icing.