ESRF	**Experiment title:** Investigation of the incorporation of an anti cancer drug in calcite for slow release applications	**Experiment number**: MD871
Beamline: ID22	**Date of experiment**: from: 11-4-15 to: 14-4-15	**Date of report**:
Shifts: 9	**Local contact(s)**: Dr. Andy Fitch	*Received at ESRF:*

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Report:

A series of calcite crystals were grown in the presence of different drugs, being the majority of them anticancer drugs.

The calcite crystals were synthesized using the vapor diffusion method, based on the dissolution of NH_3 and CO_2 gasses in a $CaCl_2$ solution containing the drug at different concentrations (Figure 1)

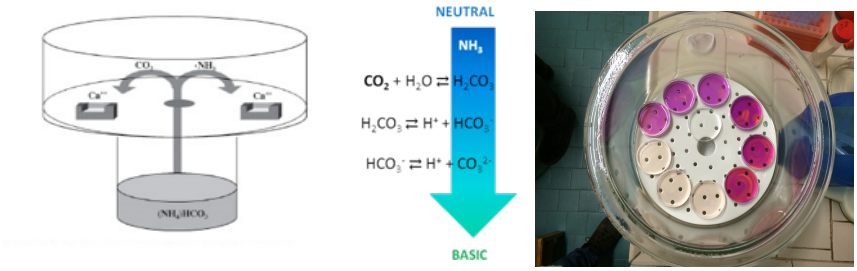

Figure 1. *From left to right* Scheme of the experimental apparatus. Chemical reactions that bring to the deposition of calcium carbonate. In the Petri dishes solution with increasing concentration (the intensity of the color increases) of doxorubicin are present.

The morphology, as well the yield of the precipitation process, was a function of the concentration of drug in the precipitating solution (Figure 2)

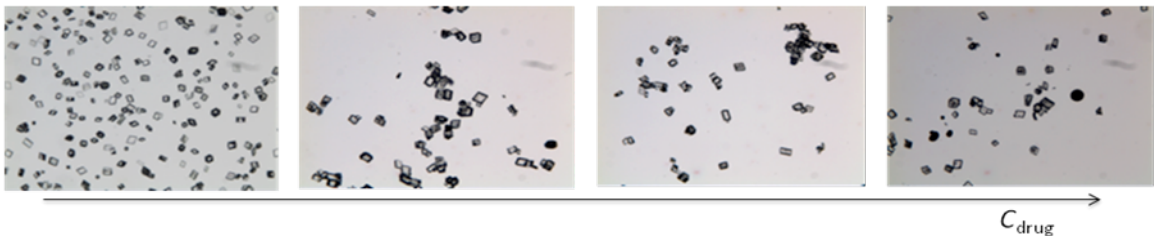

Figure 2. Optical microscope images. Change in the morphology, aggregation and density of precipitation of $CaCO_3$ crystals as function of the concentration of the drug. A similar trend was observed for all the drugs used (here doxorubicin). The average size of the crystals was about 50 μm.

The incorporation of the drug in the crystal lattice of calcite was evaluate by High Resolution X-ray Powder Diffraction Experiment at the ID22 beam line of ESRF.

The change of the lattice parameters, evaluated by the shift of the diffraction peak with respect to pure calcite, and the broadening of the diffraction peaks, were used as tool evaluate the incorporation of the drug in the calcite crystal lattice. Moreover, a thermal treatment was applied to pyrolyse the entrapped drug. After this treatment the change in the crystal lattice was removed, going back to the one of pure calcite and further proving the presence of drug in the crystalline lattice (Figure 3).

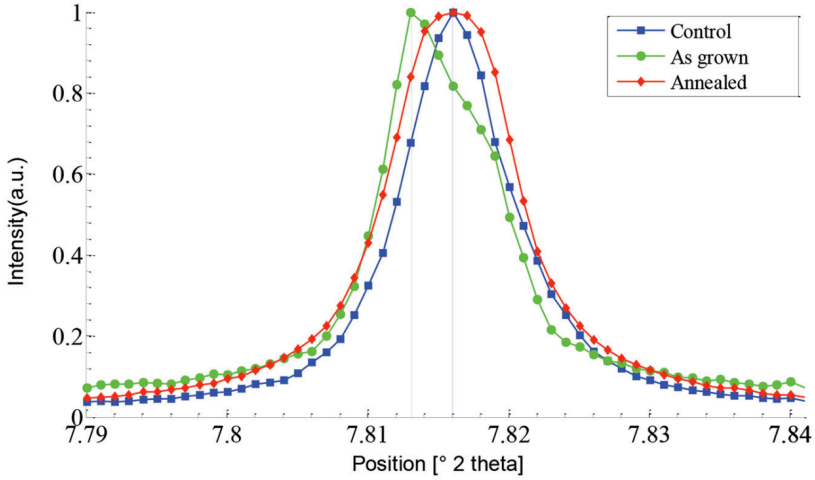

Figure 3. HRXRD profile of the {10.4} peak of calcite crystals grew in the presence of 5 mM doxorubicin. The shifht of the peak is removed after annealing, proving the presence of the drug in the crystal lattice.

The Table 1 summarizes the results of the diffraction experiments showing fro which drug a change of the lattice parameter with respect to calcite was observed.

Table 1. Summary on the entrapment of diverse drugs in the crystal lattice of calcite.

Drug	Entrapment in the crystal lattice
Doxorubicin	√
Minocilin	√
Retinoic acid	X
Dichloro acetic acid	X
Camptotecin	X
Ibuprofen	√
Fenacetin	X

In conclusion the X-ray diffraction experiment at ID22 showed that doxorubicin, minociclin and ibuprofen are incorporated in the crystal lattice of caclite.