PhD Proposal 2017

School: CentraleSupelec (campus de Châtenay)	
Laboratory: SPMS	**Web site: www.spms.ecp.fr**
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Title: Non Photochemical Light Induced Nucleation of drug. Application to polymorph, racemic and enantiomorph species
Scientific field: Material Sciences, Physical-Chemistry
Key words: nucleation, crystallization, chirality, Laser-induced

Details for the subject:

Background, Context:

Polymorphism study of pharmaceutical solid constitutes a very growing area. This is due, on the one end, to the economic pressure of the pharmaceutical industry, and on the other end to a better understanding of the polymorphism consequences on the drug properties (physical or chemical stability, solubility, dissolution rate, biodisponibility, mechanical properties, engineering process,….). Generic drug developpment has induced new studies which has established that polymophism could play a significant role in differenciation between generic and innovative form.

The understanding of some phenomenon linked to solubility and biodisponibility imply a better knowledge of molecular interactions in crystal phase and strength involved. High resolution diffraction ensure a very fine characterization of electronic and electrostatic properties of a crystal. Therefore, experimental study of polymorphism implies the perfect command of the crystallization of the required polymorph phases and the crystallization of new polymorph phases. Pr B. Garetz and AS. Myerson (USA) have established an original crystallization method (NPLIN) giving the possibility to control the polymorphism according to the polarization of the Laser beam. They have applied this new method on urea, glycine and alanine.

At CentraleSupelec we have been able to design a unique NPLIN automated experimental device [1-3] (figure 1). We have crystallized glycine [1-3, 5,6], carbamazepine [1,2,5,7] and sulfathiazole [5,7,8]

Description of the work:

We propose to control and characterize potential polymorphic phases of pharmaceutical compounds crystallized using Non Photochemical Light-Induced Nucleation for Drugs (NPLIND).

We plan to study polymorphism in different types of drug compounds. A special effort would be made to induce separate crystallization of chiral molecules from a supersaturated solution of the corresponding racemic entity. Actually, more and more chiral molecules exhibit a therapeutic effect and drug approval regulation authorities do not accept any more IND files of racemic drugs, therefore specific crystallization control of chiral molecules will become a major issue. In this project, we would like to demonstrate the feasibility of this approach at the level of the Laboratory: transposition to the pharmaceutical engineering level is not foreseen before this project is completed.

In order to understand the nucleation mechanism, fluorescent drugs will be studied at Cachan on a microfluidic device [9,11].

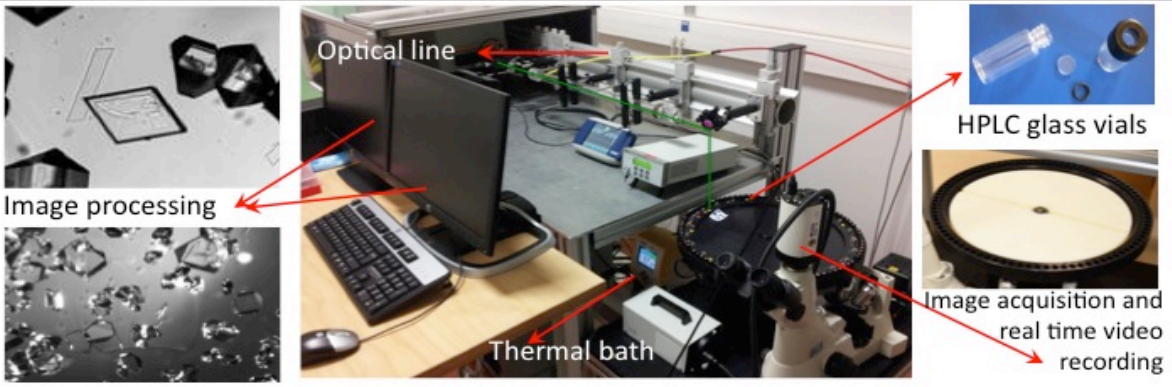

Figure 1. Experimental setup @ECP

Research subject, work plan:

The expected results in the PhD are :

- crystallization by the NPLIN method of drug polymorphs and study of the solvent polarity effect on the nucleation of the obtained polymorph phase,
- study of the enantioselectivity of drug crystallisation by NPLIN method from racemic supersaturated solutions,
- immediate characterization of the obtained phases (powder and X-Ray single crystal diffraction and Raman diffusion),
- *ab initio* determination of interaction energy the polymorph or solvate crystallized.

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