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# ADVANCED MATERIALS & PROCESSING

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### Continuous nanocrystallizing of medicaments by spray flash evaporation

The NS3E laboratory conceived the Spray Flash Evaporation (SFE) for nanocrystallizing medicaments nanoparticles in an industrial scale. The process was several times patented. The medicament to be nanocrystallized is first dissolved in a low boiling solvent. The solution is kept in a pressurized tank separated from a vacuum chamber by a heated hollow cone nozzle used to spray the liquid. The fast evaporation of the solvent is induced by the combination of the abrupt pressure drop and the high energy stored in the overheated solvent prior to nebulisation. The flash evaporation leads to nanoparticles with narrow size distribution. The nanoparticles may be composed of single compounds, mixtures of several substances or cocrystals. In the domain of medicaments, cocrystals are of high importance as they enhance bioavailability and up-take by the human body of Active Pharmaceutical Ingredients (API). Up to now, most used techniques are of batch nature and are not able to give access in big amounts to nanosized crystals or cocrystals of therapeutic interest. The SFE permits the continuous manufacturing of nano-sized cocrystals, in large amounts with a kinetic complying with the pharmaceutical industry's requirements. The efficiency of SFE is shown by the manufacturing of pure nanomedicaments but also of nano-cocrystals such as Resveratrol/4-Amino Benzamid (1/1), Caffeine/Oxalic acid (2/1) and Caffeine/Glutaric acid (1/1), with a mean particle size of between 30 and 100 nm. After showing the possibility to continuously nanocrystallize medicaments, the presentation will focus on different main challenges to further enhance the production capacity and also to understand the mechanism of SFE. Among different techniques and metrologies used or specially developed such as Phase Doppler Interferometry and AFM-TERS spectroscopies (Figure), the presentation will also focus on different crystallization configurations and scale-ups used.

### Biography

Dr. Habil. Denis SPITZER received his PHD in physical chemistry in 1993 at the University Louis Pasteur of Strasbourg. He is the founding and current Director of the NS3E Research Laboratory UMR 3208 ISL/CNRS/UNISTRA. He conducts research in continuous nanocrystallization processes of organic nanomaterials such as model medicaments and energetic materials. He is the inventor of the SFE process. He is the author of more than 150 publications and scientific reports. He received in 2013 the award of strategic thinking given by the French Homeland Minister, and more recently, in 2015, the « Grand Prix Lazare Carnot » award of the French Academy of Science, for dual use research.

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