Modular microfluidic platform for solubility measurement, nucleation statistics and polymorph screening of active pharmaceutical ingredients.

Mathilde Lambert [1,2*], Romain Grossier [1], Mehdi Lagaize [1], Thirou Bactivelane [1], Vasile Heresanu[1], Benoît Robert [2], Nadine Candoni [1], Stéphane Veesler [1]
* mathilde.lambert@univ-amu.fr
1 Centre Interdisciplinaire de Nanosciences de Marseille, CNRS, Aix-Marseille Université, CINaM-UMR7325, Campus de Luminy, Case 913, 13288 Marseille Cedex 09, France
2 Sanofi R&D – Global CMC / Synthetics – Early Development France, Impasse des ateliers, 94400 Vitry-Sur-Seine, France

Drug efficacy strongly relies on the solid state of the active pharmaceutical ingredient. Classical solid-state screening methods involve different solvent compositions and supersaturations. Moreover, the statistical approach needed to address the stochasticity of nucleation make this approach costly in material consumption. One answer is the use of microfluidics to generate hundreds of droplets (nano or micrometric volume) which are as many crystallisers in which the nucleation conditions can be varied and repeated.[1-3] This communication presents a newly developed modular microfluidic platform that provides a universal and flexible plug-and-play tool for crystallisation studies without use of surfactants. By dissolving a powder, our set-up generates saturated solutions that can be used for solubility measurements or distributed in microdroplets for crystallization studies.[4]

Here, we describe solubility measurements performed on different forms, stable and metastable, of pharmaceutical molecules (Irbesartan, Rimonabant and Aripiprazole) in organic and aqueous solvents. In addition, we provide nucleation statistics obtained for Sulfathiazole in water and in acetonitrile. Reporting polymorph screening on Sulfathiazole and statistics for nucleated forms, we find that the cooling rate influences both nucleation and polymorphism results, reflecting the competition between thermodynamics and kinetics. Three unknown forms were discovered. We also demonstrate the limitations of microfluidics for crystallisation by cooling: reducing the crystalliser volume considerably increases nucleation induction time.

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