Investigation of the shear-induced nucleation mechanism in a micro-crystallizer

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In industry, 90% [1] of the active pharmaceutical ingredients (API) are under a crystalline form. The crystallization kinetics is highly influenced both by the supersaturation conditions (temperature and concentration) and by the flow hydrodynamics [2], both thus influence the overall product quality and size. We developed a continuous seedless cooling micro-crystallizer [3]. Experiments pointed out that modification of the upstream flow conditions induces size changes of the obtained crystals [3-4], which we imputed to shear rate.

To the best of our knowledge, an in-depth knowledge of the shear-induced crystallization mechanisms is still missing. Thus, we performed a systematic analysis of the influence of the shear rate in the micro-crystallizer on the nucleation rate. We demonstrate experimentally that a nucleation rate maximum exists as a function of shear rate. We theoretically identified that shear, at first, induces the coalescence of intermediary structures which thus promote the nucleation. On the opposite, at higher shear rates, the flow induces mechanical deformation of the intermediary structures which counteracts the beneficial effect, leading to the experimentally observed non-monotonic behavior (figure 1).

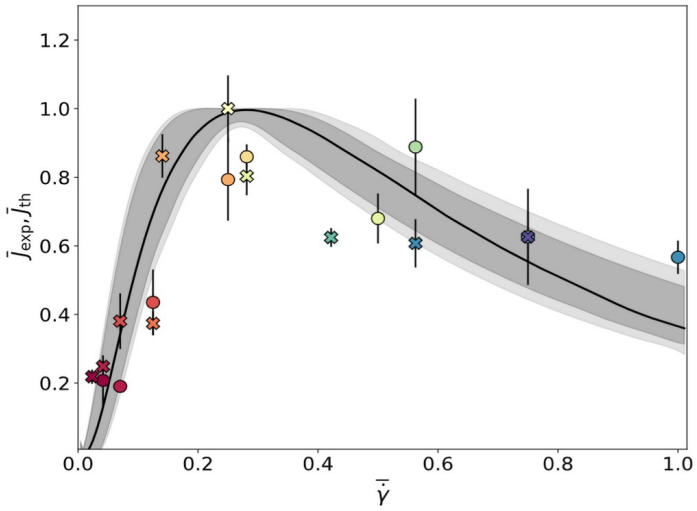

Figure 1: Influence of the shear rate on the nucleation rate of glycine

References

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