Continuous crystallization: a new option in downstream processing

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Préférence : Communication orale

Résumé

Continuous crystallization is traditionally used for large production scale (> 500 t/a)[1], using dedicated equipment (e.g. DTB, Oslo crystallizer) and mostly for evaporative crystallization. On the contrary, smaller scale crystallizations in the life-science area are generally operated batch-wise. Over the last decade and namely on the initiatives of the regulatory agencies[2], there has been increased interest on continuous crystallization at small scale, especially in the pharmaceutical manufacturing area.

The community has been mostly focusing on two types of continuous crystallizers, namely Continuous Stirred Tank Reactors (CSTR), and Plug Flow Reactors (PFR). To provide a fair assessment, several case studies using model compounds like glycine, but also active ingredients were investigated in-house and will be presented in this talk. Some of them showed advantages such as higher space-time yield, better control on particle properties, but also often generated additional issues compared to batch crystallization (e.g. continuous seeding at small scale, incrustation problems). Fortunately, these problems can be overcome by a better understanding of the crystallization process, and a careful design/selection of the crystallizer.

The results of the assessment CSTR/PFR/Batch at lab scale and a production perspective will also be presented.

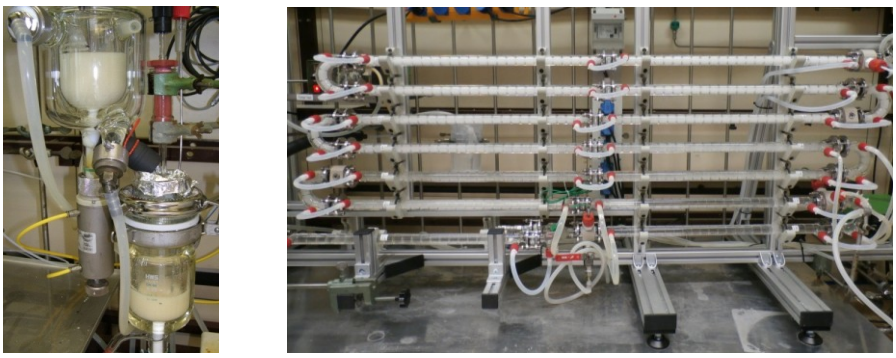

Figure 1: Example of different setups used for continuous crystallization at lab scale

Mots-clés : Cristallisation continue, principe actif, méthodes d'ensemencement

Références

1. J.M., Douglas, 1988, Conceptual Design of Chemical Processes, McGraw Hill.

2. S. Chatterjee, 2012, FDA perspective on continuous manufacturing. Accessed October 8th, 2015 from http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/UCM341197.pdf.