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# Continuous-flow microfluidic nanoprecipitation for poorly soluble drug encapsulation in polymeric nanocarriers with tunable release properties

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Polymeric drug-loaded nanoparticles are attracting a growing interest due to their potential use for bioengineering, nanomedicine and therapeutic applications. Their typical dimension (10-1000 nm) allow them to penetrate living tissues, encapsulate, protect and deliver a drug; not to mention the possibility to functionalize macromolecular chains for site recognition, drug binding and drug release (stimuli responsive polymers). The fabrication of smart functional drug-loaded polymer nanoparticles coupled with advanced chemical manipulation in order to impart biological biocompatibility and recognition is thus becoming an emerging field.

In light of the above mentioned statement, we have developed an integrated and intensified microprocess for the continuous-flow synthesis of (co)polymers and colloidal suspension of drug-loaded polymeric nanoparticles. This microprocess includes a synthesis platform (CMS), an online analysis platform for the continuous monitoring of (co)polymer characteristics (COA) and a post processing unit allowing encapsulation of a given drug (IPR).

The synthesis platform relies on the use of microtubular reactors and micromixers to benefit from intensified heat and mass transfers. Controlled/'living' polymerization reactions have mainly been performed in order to design various polymer architectures, such as linear, block or branched (co)polymers. The obtained polymer solution is then mixed with a solvent solution admixed with a given amount of drug and the resulting diluted polymer/drug solution is nanoprecipitated with a polymer non-solvent solution leading ultimately to the production of a colloidal suspension of drug-loaded nanoparticles. The online analysis platform, so-called CORSEMP (Continuous Online Rapid SEC Monitoring of Polymerizations) includes a GPC column and a train of 5 detectors (RI, UV, LS, capillary viscosimeter, ELS). The system allows a continuous automatic sampling and 'near real-time' monitoring of the raw (co)polymer characteristics, such as molecular weight and molecular weight distribution. This microprocess appears well-adapted to produce polymeric nanoparticles libraries and to assess the effects of stepwise modifications of operating and composition parameters (residence time, temperature, reactants concentrations, flow rate ratio between polymer and non-solvent solution) over nanoparticles drug release properties.

The lecture will first emphasis the influence of the flow rate ratio (R) between the non-solvent and diluted polymer solutions, the architecture of poly(methyl metacrylate) (linear and branched),its concentration and the type of micromixer used in the post processing unit on the size of the nanoparticles. Then le lecture will address the drug release properties of these nanoparticles showing that a sustain release of a poorly soluble drug (ketoprofene) can be achieved over 24 hours and that the release profile is highly affected by the size of the nanoparticles. Therefore it will be demonstrated that tunable drug release of poorly soluble drugs can be readily achieved by adjusting the appropriate operating and composition parameters of the aforementioned microprocess.

## Biography

Christophe A Serra is Professor at the University of Strasbourg teaching at the European School of Chemistry, Polymers and Materials Science (ECPM). He received his MS and Ph.D. degrees in chemical engineering from the National Engineering School of the Chemical Industries (Nancy) and Paul Sabatier University (Toulouse), respectively. His researches concern the development of intensified and integrated microfluidic-assisted polymer processes for the synthesis of architecture-controlled polymers and functional microstructured polymer particles.

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