A new approach to control nucleation of crystals based on engineered drug carrier nanoparticles using a co-flow microfluidic device

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The purpose of this study was to develop a new approach to tailor crystal size based on the formation of acetaminophen encapsulated polymeric nanoparticles by nanoprecipitation ("diffusion-stranding" process) using a co-flow microfluidic device. The polymer additive is expected to reduce the nucleation rate [1], whereas the nanometer size range of the particles allows for efficient uptake by a variety of cell types without causing an embolism [2]. In this study, polycaprolactone (PCL) was chosen as a carrier for nanoparticle fabrication, because it is a biodegradable and bioresorbable polymer commonly used in pharmaceutical industry [3], while tetrahydrofuran (THF) was used as a water-miscible volatile solvent [4]. Nanoparticles were fabricated in a glass capillary device consisted of coaxial assembly of round and square capillaries glued onto the surface of a microscope slide. The organic phase containing 0.1 % (w/w) polymer and 0.02- 0.07 % (w/w) acetaminophen in THF was injected through the inner capillary tube with a tapered cross section culminated in a circular orifice. The water phase containing 0.1 % (w/w) Tween 80 (surfactant) was delivered co-currently through the outer square capillary. The organic phase formed a microscopic jet of controllable size in the aqueous phase and the particles were formed by counter-current diffusion of water and THF at the water-organic phase interface. Due to transparent walls of the capillaries, the process was observed by a high-speed camera. Microfluidic devices with an orifice size of 200 µm were fabricated and the particle generation process for each orifice size was investigated using five different aqueous to organic phase ratios, Q_{aq}/Q_{or} (1.5, 3.0, 4.5, 7.0, and 10.0). The experimental set-up is depicted in Fig. 1. The nanoparticles were produced with a mean size of 238−326 nm and a drug entrapment efficiency between 21.3 % and 77.5 %, depending on the acetaminophen content and Q_{aq}/Q_{or} value.

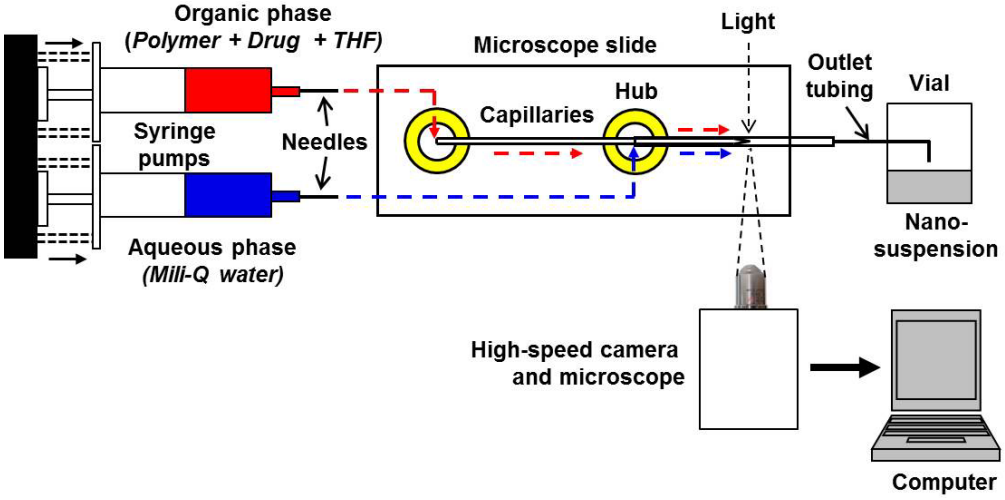

Fig. 1: Schematic diagram of the experimental setup used in this work

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