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Enhanced yield and purity in API Crystallisation with a new application of microengineered membrane system for the formation of uniform nanocrystals size distribution and smooth crystal surface

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The purpose of this study was to introduce a new approach of micro-engineered membrane system which has a perfect hexagonal array of uniform pores to tailor size of biodegradable and bioresorbable drug-excipient based on the formation of polymeric nanoparticles (NPs) by solvent-displacement (nanoprecipitation) method [1]. This system induced a rapid mixing process to control and limit the maximum level of supersaturation needed for nucleation due to defined mass transfer across the membrane, which allows for the generation of more nuclei and smaller size of NPs [2]. In this study, polycaprolactone (PCL) was chosen as a drug-carrier for nanoparticle fabrication due to its slow degradation, biocompatibility, having Food and Drug Administration (FDA) approval and commonly applied in pharmaceutical industry [3], while acetone (Ace) was used as a water-miscible volatile solvent (ICH, Class 2) [4]. Nanoparticles were produced instantaneously by fast diffusion once the organic phase is introduced through the membrane pores coming into contact with the aqueous phase that flows tangentially to the membrane surface. The organic phase containing 0.3 – 0.6 % (w/w) polymer in Ace was injected through the nickel micro-engineered membrane at different dependent experimental parameters; (i) organic phase injection rates (2 – 5 ml/min), (ii) agitation speeds (200 – 1300 rpm) and (iii) aqueous phase to organic phase volume ratios, \(V_{\text{aq}}/V_{\text{or}}\) (1.5, 3.0, 4.5, 7.0, and 10.0). The water phase containing 1 % (w/w) polyvinylalcohol (PVA) as a hydrophilic surfactant was filled in the stirred cell with 20 – 60 ml until a predetermined \(V_{\text{aq}}/V_{\text{or}}\) was achieved. The membranes containing uniform cylindrical pores we applied with a diameter of 10, 20 and 40 \(\mu\)m, arranged at a uniform spacing of 200 \(\mu\)m. The experimental set-up is depicted in Fig. 1. The nanoparticles were produced with a mean size of 205 – 276 nm depending upon the shear stress at the membrane surface caused by different values in stirring speeds. The physical characterisations of formulated nanoparticles were certainly proved by the X-ray diffractometry (XRD), differential scanning calorimetry (DSC) and Attenuated total reflection-Fourier transform infrared (ATR-FTIR).

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