FORMATION OF FUNCTIONAL PHARMACEUTICAL NANOPARTICLES USING MEMBRANE DISPERSION CELL COMBINED WITH SOLVENT DISPLACEMENT METHOD

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The purpose of this study was to develop a new solvent-displacement (nanoprecipitation) method [1] based on a micro-engineered membrane with a regular array of uniform pores to tailor the size of biodegradable and bioresorbable drug-loaded polymeric nanoparticles (NPs). Polycaprolactone (PCL) was chosen as a Food and Drug Administration (FDA) approved drug carrier, commonly applied in pharmaceutical industry [2] due to its slow degradation rate and biocompatibility, while acetone (Ace) was used as a water-miscible volatile organic solvent (ICH, Class 2) [3]. A natural macrocyclic lactone, rapamycin (RAPA) which is also known as a potent immunosuppressive agent [4] was used in the encapsulation experiment and drug release study. Nanoparticles were produced instantaneously by fast solvent switching once the organic phase was injected through the membrane pores into a stirred aqueous phase. The organic phase was made up of 0.3 − 0.6 % (w/w) PCL in Ace and the aqueous phase was consisted of 1 % (w/w) polyvinylalcohol (PVA) dissolved in Milli-Q water. The cell was filled with 20 − 60 ml of the aqueous phase and the organic phase was injected until a predetermined aqueous phase to organic phase volume ratio, V_{aq}/V_{or} was achieved. The parameters that have been varied in the experiments were: (i) organic phase injection rate (2-5 ml/min), (ii) agitation speed of the stirrer (200-1300 rpm) and (iii) final volume ratio, V_{aq}/V_{or} (1.5, 3.0, 4.5, 7.0, and 10.0). The membrane had uniform cylindrical pores with a diameter of 10, 20 and 40 μm, arranged at a uniform spacing of 200 μm. The experimental set-up is depicted in Fig. 1. The nanoparticles were produced with a mean size of 156−276 nm depending on the shear stress at the membrane surface controlled by the stirring speed and other parameters. The physical characterisations of formulated nanoparticles were determined by X-ray diffractometry (XRD), differential scanning calorimetry (DSC) and Attenuated total reflection-Fourier transform infrared (ATR-FTIR) spectroscopy.

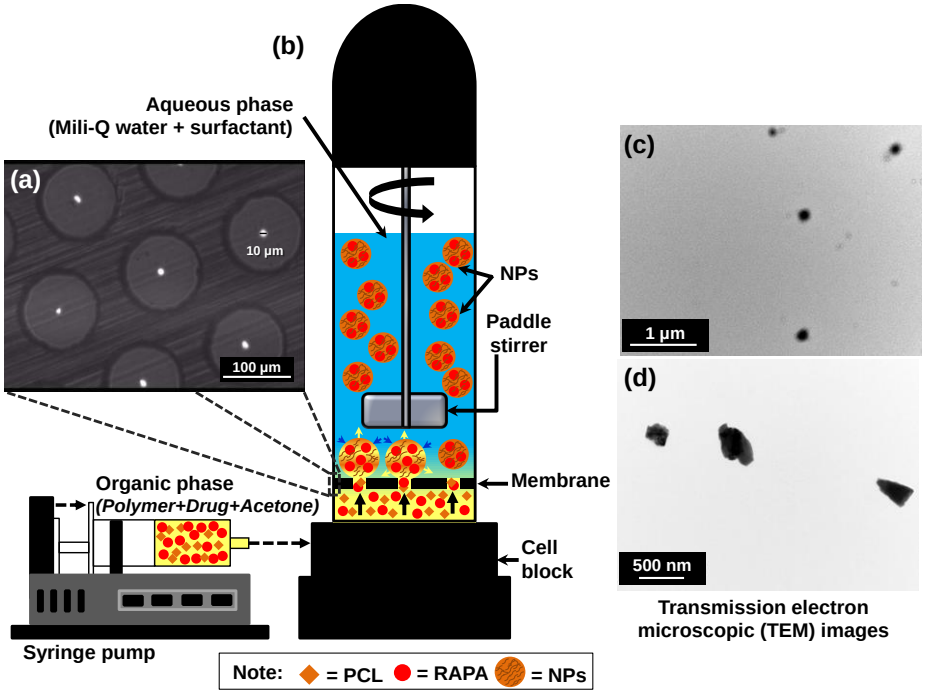

Figure 1 – (a) A photomicrograph of 10 μm nickel micro-engineered membrane. (b) *Schematic diagram of the experimental setup used in this work. (c) TEM image of RAPA-PCL encapsulated nanoparticles. (d) TEM image of RAPA- without PCL NPs host.*

[1] H. Konno, & L.S. Taylor, *Pharm. Res.***2008**, 25, 969-978.
[2] M.A. Woodruff & D.W. Hutmacher, *Prog. Polym. Sci.***2010**, 35, 1217−1256.
[3] B.V.N. Nagavarma, et al., *Asian J Pharm. Clin. Res.* **2012**, 5, 16−23.
[4] Y.K. Joung, et al., Biomater. Biomed. Eng. **2014**, 1, 13-25.