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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.

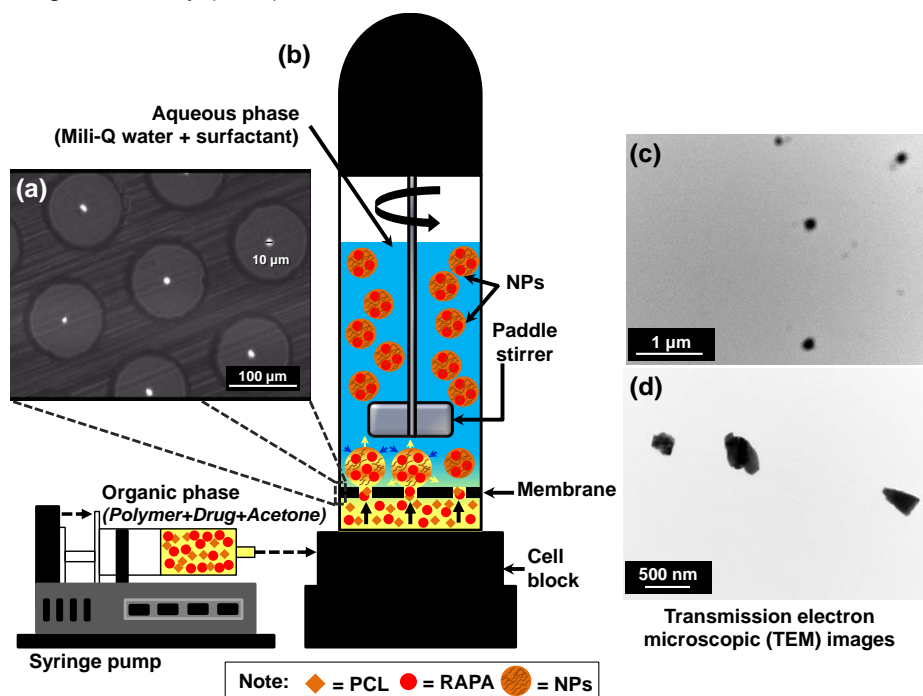


Figure 1 – (a) A photomicrograph of 10 μm nickel micro-engineered membrane. (b) Schematic diagram of the experimental setup used in this work. (c) TEM image of RAPA-PCL encapsulated nanoparticles. (d) TEM image of RAPA- without PCL NPs host.

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