A new advanced membrane technique for the formation of highly uniform functional nanoparticles with tailored properties suitable for high-value pharmaceutical applications

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1. Research highlight: What is functional nanoparticle?

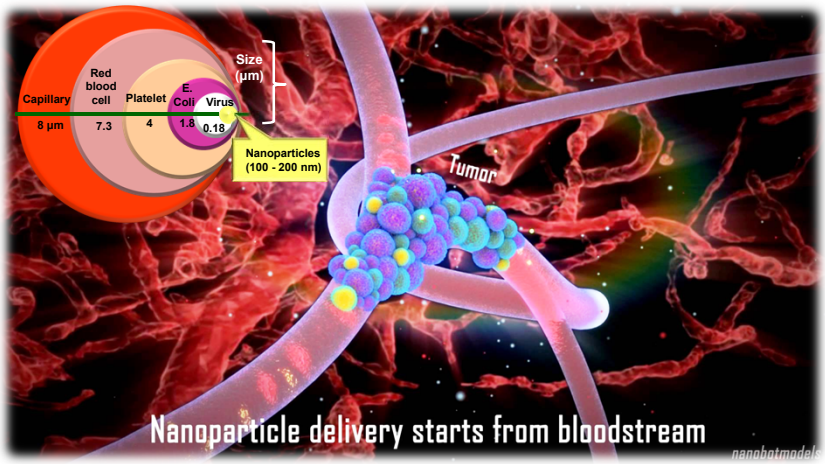

Fig. 1: Functional NPs administration route mechanism depending on their particle size without causing an embolism.

Functional nanoparticles (NPs) are scientifically defined as solid, colloidal particles or carriers in the range 10-1000 nm [1] with numerous functions such as; (i) protections of active ingredients (drugs) against degradation, (ii) targeting of drugs to specific sites of action (organ or tissue), and (iii) delivery of biological molecules such as proteins, peptides and oligonucleotides depending upon their administration routes either orally, parenterally or locally [2].

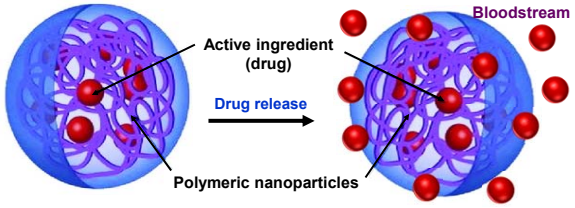

Fig. 2: Drug release mechanism from NPs carrier.

2. New advancement techniques: Membrane system & nanoprecipitation method

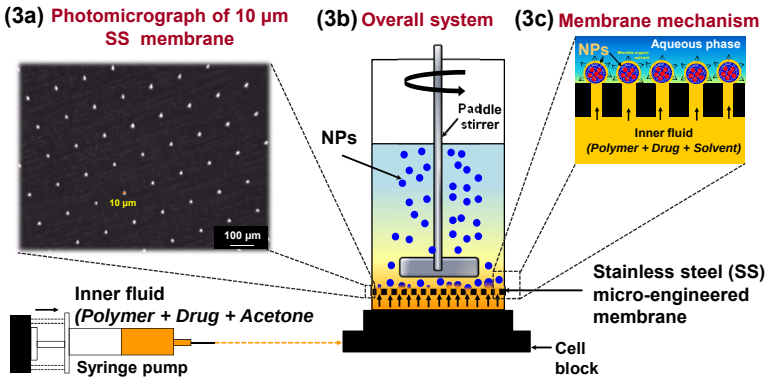

Fig. 3: Schematic diagram of the experimental setup.

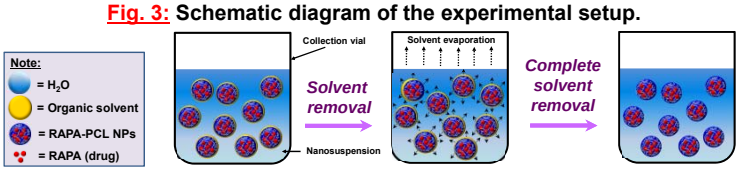

Fig. 4: Solvent removal mechanism of final polymeric NPs product.

NPs were produced instantaneously by fast diffusion (nanoprecipitation) once the organic phase is introduced through the membrane pores coming into contact with the aqueous phase that flows tangentially to the membrane surface.

3. Materials and parameters setting

Table 1. Experimental materials/parameters.

Subjects	Materials/Properties	Compositions/Remarks
Aqueous phase	Mili-Q-water + surfactant	(Depending on V_{aq}/V_{oq})
Organic phase	Dissolved mixture of polycaprolactone (PCL) + drug (rapamycin) in acetone	6 g/l PCL + 40 w/w% rapamycin (RAPA)
Membrane	Pore size = 10 µm	Stainless steel (SS) membrane
Optimum exp. parameters	(i) Volume ratio (V_{aq}/V_{or}) (ii) Stirring speed (rpm) (iii) Injection rate (ml/min)	(i) 10.0 (ii) 1300 rpm (iii) 5 ml/min

4. NPs physical characterisations & images

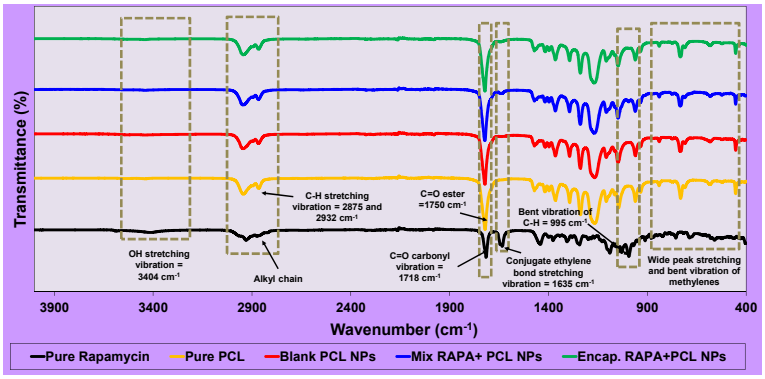

Fig. 5: Attenuated total reflectance Fourier transform infrared (ATR-FTIR) spectrums elucidated that rapamycin , RAPA (drug) was successfully embedded (encapsulated) onto NPs polymer matrix with 98.9 % encapsulation efficiency.

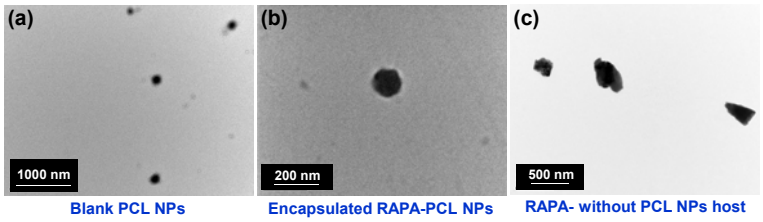

Fig. 6: Transmission electron microscopy (TEM) images of uniform spherical RAPA-encapsulated PCL NPs within particle size < 200 µm, polydispersity index (PDI) < 0.1 (highly monodispersed particles) produced at the optimum experimental conditions (refer to Table 1).

5. Conclusions

- Micro-engineered membrane system is shown to be convenient for production of highly controllable size of NPs that can be applied as a drug carrier with any substitution elements (*eg*: drug or nanofillers).
- The higher the aqueous-to-organic volume ratio, the higher the dilution factor of the polymer in the liquid phase and the lower the rate of particle growth after nucleation, resulting in smaller particle size.

Acknowledgements

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References: [1] Charcosset, et al. (2010). *Ind. Eng. Chem. Res.* 49, 5489−5495, [2]. Konno & Taylor (2008). *Pharm. Res.* 25, 969−978.