Engineering and Physical Sciences Research Council

Formulation for 3D printing: Creating a plug and play platform for a disruptive UK industry

RC: 2

Project: Jet mixing - towards continuous production of core-shell particles for additive manufacturing

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INTRODUCTION

Use of jet mixing products in selective laser sintering (SLS)

Selective laser sintering uses laser power to fuse powder particles together. It creates **parts with superior mechanical properties and** enables creation of more **complex geometries**. However, use of SLS in pharmaceutical and biomedical industry is hampered by the **lack of sintrable polymeric materials**. This can be overcome by the synthesis of core-shell particles with shell made of sintrable polymer, and core consisting of a non-sintrable one. Such particles can be pre-formulated as emulsion, through process of jet mixing. If emulsion contains photopolymerisable monomer as a dispersed phase, these droplets can be converted to solid particles by UV curing.

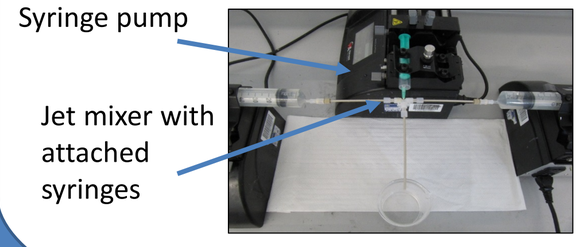


Image 1. Jet mixing setup

ADVANTAGES OF JET MIXING

- Creation of **core-shell** particles in **micro** and **nano** size-range
- Potential for continuous production in amounts of up to **several kg/day**
- **Fast, cheap** and **easy** assembly
- It's components are compatible with **most solvents**, **polar and nonpolar**

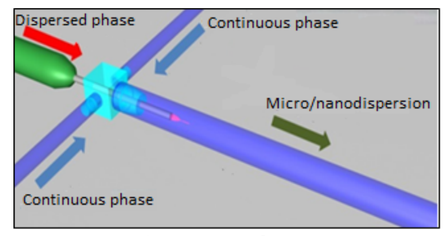


Image 2. Schematic of a jet mixer

AIM

To **establish a jet mixing platform** for the **production of core-shell particles** and to utilize as-produced particles in **SLS of biomedical products.**

1. Assembling the jet mixing apparatus. Preparation of core-shell particles with liquid cores.
2. Manufacturing core-shell particles with solid (photocured) cores. Incorporation of a model drug in the core.
3. Use SLS to fabricate a biomedical product from the solid core-shell particles with incorporated drug.

RESULTS

(1) Core-shell particles with liquid cores

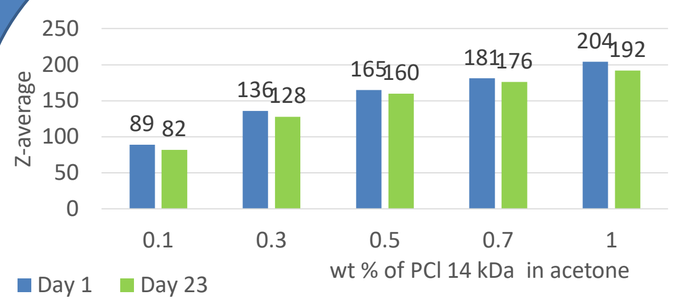


Chart 1. Comparison of particle size after 1 and 23 days at RT for nanocapsules created by acetone-water nanoprecipitation from solutions with different wt % of PCL 14 kDa in acetone

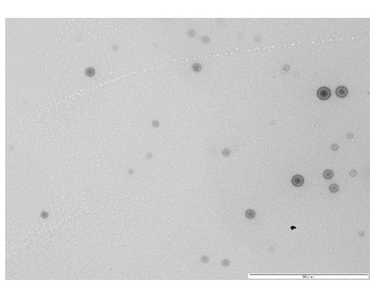


Image 3. TEM image of PCL nanocapsules (1% PCL in acetone) after 1 day at RT; negatively stained with uranyl acetate

Synthesised nanoparticles with shell made of:
•PCL • PS • PLA • PMMA

(2) Core-shell particles with solid cores

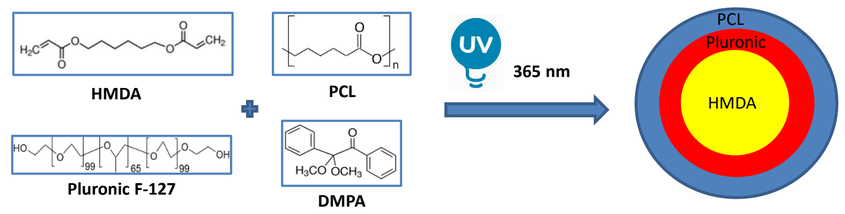


Image 4. Schematic of the structure of solid core-shell particles

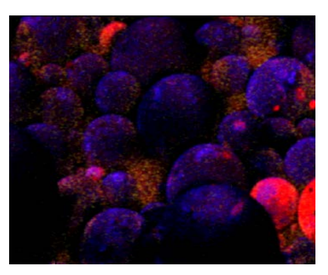


Image 5. ToF-SIMS analysis of the surface composition of PLC-Pluronic-HMDA particles

(PCL, Pluronic F-127)

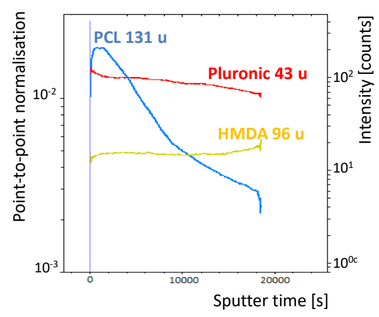


Image 6. Depth profiling of PCL-Pluronic-HMDA particles, outer layers, Ar^+_{1500}, 10 keV, 5 nA

(3) Core-shell particles with solid cores: suitability for SLS

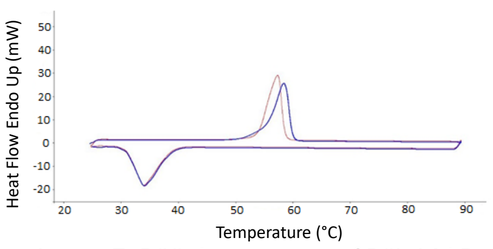


Image 7. DSC thermogram of PCL 14 kDa showing 2 heating and cooling cycles performed at the rate of 10°C/min

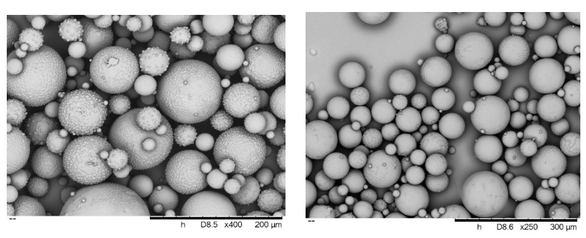
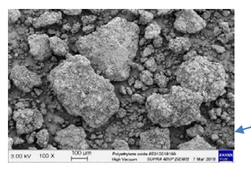


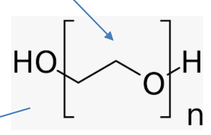
Image 8. SEM scan of PCL-Pluronic-HMDA particles to be sintered

- Shell materials (PCL and Pluronic): same melting range
- **Low melting temperature and wide sintering window** of shell
- Spherical shape – optimal flow inside a build chamber
- Average **particle size 50 - 70 µm**

(4) SLS of solid core-shell particles

- Particles **sintered individually and in blend with Polyox N80** (similar meling range, fablet filler)





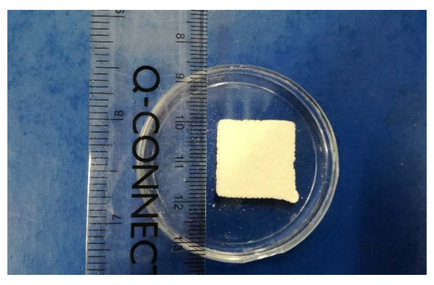


Image 9. Sintered blend of PCL-Pluronic-HMDA particles and Polyox N80 (1:1), 3 layers sintered

- Particles sintrable alone and in combination with Polyox N80 (1:1 ratio)
- In combination with Polyox – **enhance** its **flow** and **reduce warping**

CONCLUSIONS

- Jet mixer reproducibly synthesises nanoparticles ($d_{average}$ = 80-200 nm) from PCL, PLA, PMMA and PS, through process of flash nanoprecipitation.
- Jet mixer reproducibly synthesises solid core-shell microparticles ($d_{average}$ = 50-70 µm), with core made of photocurable material (HMDA) and shell consisting of layers of Pluronic F-127 and PCL. Layered tructure of the particles is confirmed by ToF-SIMS analysis.
- Particles are sintrable individually and in blends with excipient Polyox N80, which demonstrates their potential for use in SLS of pharmaceutical products.

FUTURE WORK

- Swapping HMDA for a biodegradable photocurable core polymer.
- Incorporation of model drug (ibuprofen) in the particle core and SLS of as produced particles.
- Dissolution and stability testing of the sintered products.

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