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Development of Novel Drug Formulation Using Microfluidic Device

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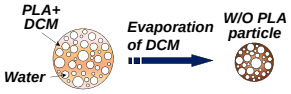
1. Introduction

Biosorbable poly(lactic acid) (PLA) microspheres have been used for controlled drug release, as ultrasound contrast agents, for cell cultivation in tissue engineering, fabrication of scaffolds, composite coatings, etc. Coherent PLA particles can be fabricated via single emulsion route. First, PLA is dissolved in a volatile organic solvent (DCM) and this solution is emulsified in an aqueous surfactant solution. In the next stage, the resultant droplets are solidified by evaporation of solvent. Porous PLA particles can be produced via W/O/W emulsion route, where first, an inner water phase is dispersed in a mixture of PLA and DCM in the presence of oil-soluble surfactant form a W/O emulsion. This emulsion is then dispersed drop-wise into an aqueous surfactant solution to form a W/O/W emulsion. W/O particles are formed by evaporation of DCM.

(a) Single emulsion method

(b) Multiple emulsion method



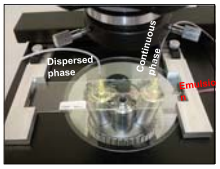
2. Emulsion Formulation

Single o/w) emulsion method:

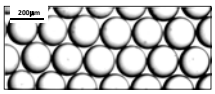
-Continuous phase: 5 wt.% poly(vinyl alcohol) in Milli-Q water
-Dispersed phase: 0.5–3% wt. poly(dl-lactic acid) + trace amounts of Nile red dye in organic solvent (dichloromethane, ethyl acetate, 1:2 chloroform/toluene)

Multiple w/o/w) emulsion method:

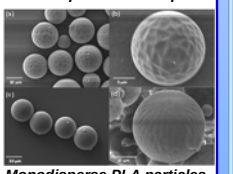
-Outer aqueous phase (a & b): 5 wt.% poly(vinyl alcohol) in Milli-Q water
-Oil phase (a): 10 wt.% PGPR + 1 wt.% PLA + Nile red in DCM
-Inner aqueous phase (a): 20 wt.% Milli-Q water
-Oil phase (b): 10 wt.% PGPR + 1 wt.% PLA + Nile red in 1:2 chloroform/toluene
-Inner aqueous phase (b): 10 wt.% Milli-Q water



Experimental setup



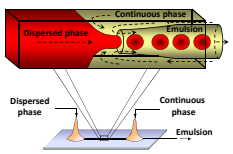
Monodisperse PLA droplets

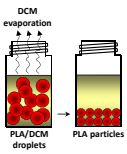


Monodisperse PLA particles

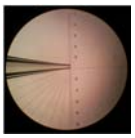
3. Glass Capillary Devices [1]

The dispersed and continuous phase were supplied from the two ends of the same square capillary in opposite directions and both liquids were collected through the inner circular capillary. The continuous phase moulds the interface into a cusp, which causes the dispersed phase to break into drops in the tapered section of the collection tube. Taper angle and aperture size of inner capillaries was finely tuned with a micropipette puller and microforge. Capillary tips were treated with a hydrophilic silane to hydrophilise the glass surface uniformly.



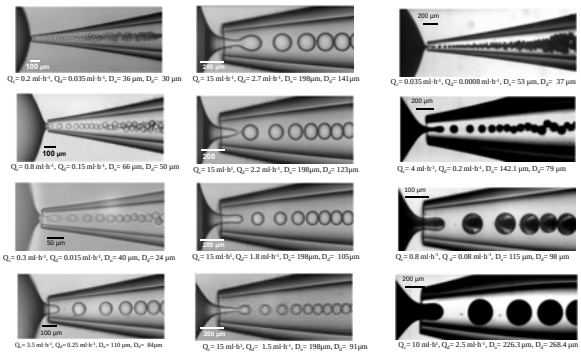


Capillary Shaping in Microforge



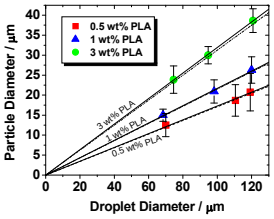
4. Drop Generation in Glass Capillaries

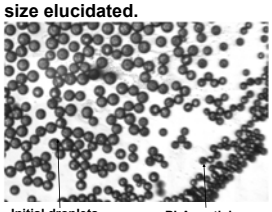
(a) Single Emulsions *(b) Multiple Emulsions*



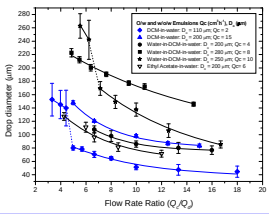
5. Experimental Results

Results show linear relationship between particle and droplet size; gradient increases when PLA concentration is higher. Solid lines represent trend lines; dotted lines are lines corresponding to mass balance equations.
Relationship between flow conditions and optimal drop size elucidated.





Initial droplets PLA particles



6. Conclusions

- **Monodispersed poly(lactic acid) (PLA) particles of 10 to 40 μm have been produced via flow focusing glass capillary devices.**
- **The sizes of PLA particles has been accurately controlled with a selection of PLA concentration in DCM (0.5–5 wt.%), orifice size of the injection capillary and fluid flow rates.**
- **Further work will investigate drug release profile for these particles.**

7. Acknowledgement

This work was supported by EPSRC first grant No. EP/HO29923/1

Reference **[1] A.S. Utada *et al*., Monodisperse double emulsions generated from a microcapillary device, *Science* 308, 537 (2005).**

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