
This item was submitted to [Loughborough's Research Repository](#) by the author.
Items in Figshare are protected by copyright, with all rights reserved, unless otherwise indicated.

Microparticles production for drug delivery using glass microfluidic devices

PLEASE CITE THE PUBLISHED VERSION

<http://www.ukptforum.org.uk/index.htm>

PUBLISHER

© The Authors

VERSION

AM (Accepted Manuscript)

PUBLISHER STATEMENT

This work is made available according to the conditions of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) licence. Full details of this licence are available at:
<https://creativecommons.org/licenses/by-nc-nd/4.0/>

LICENCE

CC BY-NC-ND 4.0

REPOSITORY RECORD

Ekanem, Ekanem E., and Goran T. Vladislavljevic. 2015. "Microparticles Production for Drug Delivery Using Glass Microfluidic Devices". figshare. <https://hdl.handle.net/2134/19007>.

MICROPARTICLES PRODUCTION FOR DRUG DELIVERY USING GLASS USING GLASS MICROFLUIDIC DEVICES

Ekanem E. Ekanem, Goran T. Vladisavljevic
Loughborough University, Loughborough, LE11 3TU, United Kingdom.

Production of biodegradable particles of poly(lactic acid) (PLA) and poly(lactic-co-glycolic acid), which serve as drug encapsulants with modifiable internal and surface microstructures, have been achieved by emulsification using microfabricated 3D (axisymmetric) flow focusing glass capillary microfluidic devices and subsequent solvent evaporation.

Flow focusing glass microfluidic devices pioneered by Utada et al. (2005) consist of coaxial assembly of glass capillaries glued onto a microscope slide. Unlike other microfabricated devices with a flow focusing geometry, the symmetrical enveloping of the dispersed phase by the continuous phase is enabled by 3-D (axisymmetric) microfluidic flow focusing devices as a result of the circular cross section of the orifice possessed by its collection channel or capillary. Hence, monodispersed droplets are facilely generated from the devices. By varying this orifice size and manipulating the flow rates of the dispersed and continuous phase, size-tunable droplets have been generated and transformed into monodispersed particles after droplet evaporation (Vladisavljević et al., 2014).

In this work, these unique properties were exploited to flow focus a dispersed phase consisting of a polymer dissolved in a volatile organic solvent (ethyl acetate or dichloromethane) by a countercurrent flowing continuous phase, consisting of 5% (w/w) aqueous poly(vinyl alcohol) solution. As shown in Figure 1, the continuous and dispersed phases were pumped to the device counter-currently using separate syringe pumps. The droplets, totally enveloped by the continuous phase, were collected through a collection capillary with a tapered cross section and vacuum evaporated to form particles Figure 2(a). The drop generation process was recorded using a high-speed camera attached to an inverted microscope for droplet generation monitoring and post-generation analysis. By introducing a phase change material for the polymer in the dispersed phase, golf ball-like particles Figure 2(b) with adjustable porosities/surface morphologies were produced after droplet evaporation in a single step without pre-emulsification of the dispersed phase (Vladisavljević et al., 2014) or post emulsification polymerization (Zhou et al., 2011). Also, unlike particles produced from conventional and tubular coflow emulsification techniques used in (Kim, Lee, Park, & Cho, 2010) and (Hwangbo, Kim, Lee, & Cho, 2011) respectively, the production of higher grade microspheres from uniform, size-controllable and generation rate-controllable droplets of both single and multiple emulsions is enhanced by glass microfluidic devices. Furthermore, for the formation of nanoclay embedded microparticles, the microstructural differences in microparticles produced after droplet evaporation when nanoclay was introduced into the dispersed phase was investigated for the formation of nanoclay embedded microparticles (Figure 2(c)). As a further step to demonstrate the suitability of these devices to produce particles which serve as vehicles for drug encapsulation in drug delivery, when a hydrophobic drug was dissolved in the dispersed phase of ethyl acetate, controlled drug release was observable over 120 hours. Also, release modification as a result of

microstructural differences in golf ball like and nanoclay embedded particles were also investigated. Although glass capillary devices cannot easily be replicated as those made from mouldable polymers such as polydimethylsiloxane (PDMS), they are more chemically and mechanically robust than PDMS devices, do not swell, and the size of entry orifice can be precisely controlled by a micropipette puller to produce droplets of tuneable size.

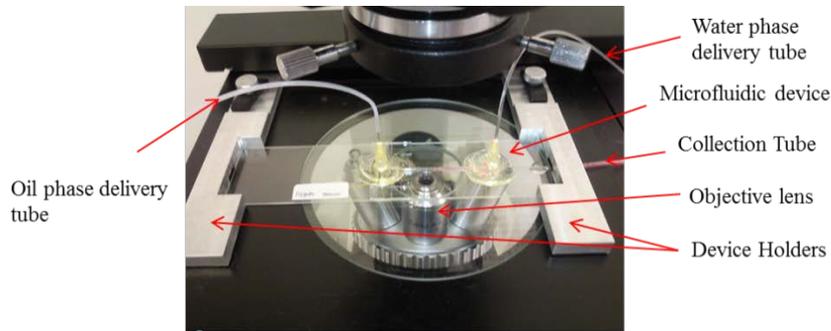


Figure 1: Experimental set-up used in this work for microfluidic production of emulsions.

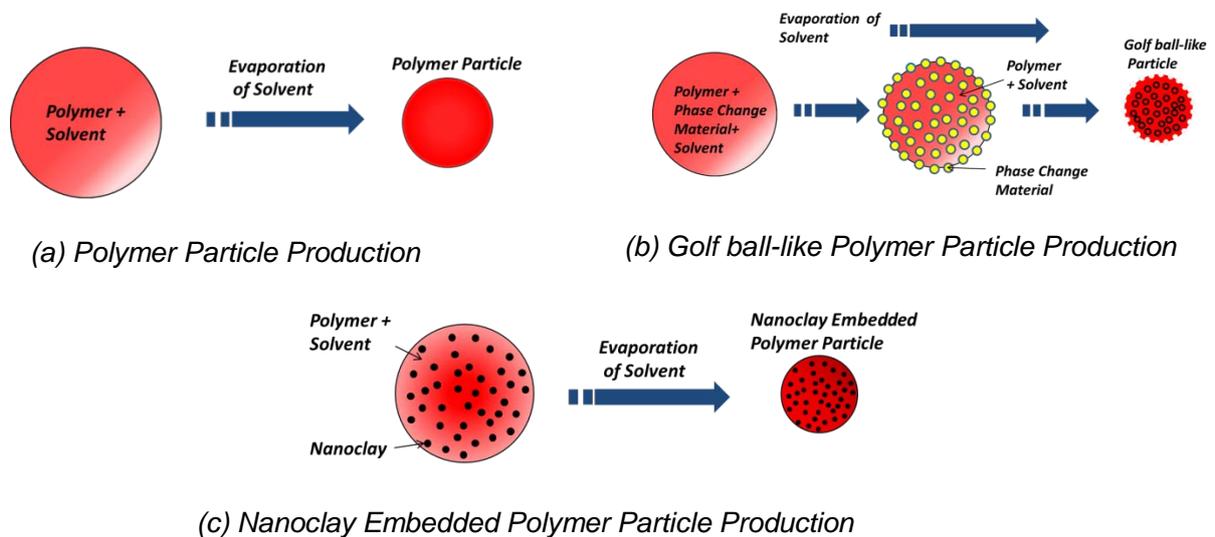


Figure 2: Microparticle formation from microdroplets

REFERENCES:

Hwangbo, K.-H., Kim, M. R., Lee, C.-S., & Cho, K. Y. (2011). Facile fabrication of uniform golf-ball-shaped microparticles from various polymers. *Soft Matter*, 7(22), 10874.

Kim, M. R., Lee, S., Park, J.-K., & Cho, K. Y. (2010). Golf ball-shaped PLGA microparticles with internal pores fabricated by simple O/W emulsion. *Chemical communications (Cambridge, England)*, 46(39), 7433–5.

Utada, a S., Lorenceau, E., Link, D. R., Kaplan, P. D., Stone, H. a., & Weitz, D. a. (2005). Monodisperse double emulsions generated from a microcapillary device. *Science (New York, N.Y.)*, 308(5721), 537–41.

Vladislavljević, G. T., Shahmohamadi, H., Das, D. B., Ekanem, E. E., Tauanov, Z., & Sharma, L. (2014). Glass capillary microfluidics for production of monodispersed poly (dl-lactic acid) and polycaprolactone microparticles: Experiments and numerical simulations. *Journal of colloid and interface science*, 418, 163–70.

Zhou, Q., Xiang, H., Fan, H., Yang, X., Zhao, N., & Xu, J. (2011). Facile fabrication of golf ball-like hollow microspheres of organic-inorganic silica. *Journal of Materials Chemistry*, 21(34), 13056.