3MDGen—High Throughput Droplet Generation

Z. Halvorsen, V. Revol, N. Schmid

A high throughput microfluidic device to produce highly uniform micro-droplets has been developed. Micro-droplets with a narrow size distribution have applications in the fields of pharmaceutics, cosmetics, diagnostics and the food industry. The narrow size distribution of emulsions increases their stability and allows a high degree of control over volumes, payload and tailored release of encapsulated substances.

Micro-emulsions could be formed when two or more immiscible liquids like water and oil are mixed, so that one liquid forms droplets in the other liquid and stabilizes with the help of an added surfactant (amphiphilic molecules that act as an emulsifier). This technology can be used for protection from heat, moisture and oxidation as well as to increase the stability of compounds, to mask undesirable tastes and to improve the release properties of compounds like target delivery in food and pharmaceutical industries. [1,2]

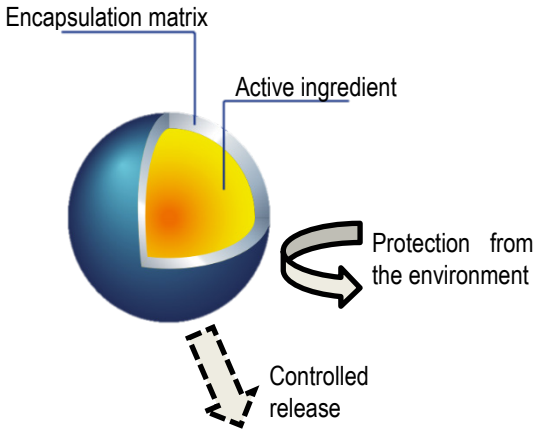

Figure 1: Motivation for encapsulation of active compound.

In this project we fabricated a membrane emulsification device, similar to the grooved microchannel (MC) array developed by Prof. Mitsutoshi Nakajima [3] to manufacture emulsions with narrow size distribution, which provides a very high control over the drop formation. Water in oil or oil in water single emulsion drops were manufactured by changing the surface chemistry of the microchannel to hydrophobic or hydrophilic, respectively. The coefficient of variation of the drop size is as low as 3%

Poly (lactic- co-glycolic acid) (PLGA) is well established as a biodegradable polymer carrier for drug encapsulation and drug-depot delivery. In order to have a high degree of control over beads degradation rate and ultimately drug release, highly monodispersed beads are required. Conventional methods of PLGA particles synthesis with high shear force mixing generates beads with a very wide range of diameters, which is not desirable and size selection for the emulsion particles is also limited.

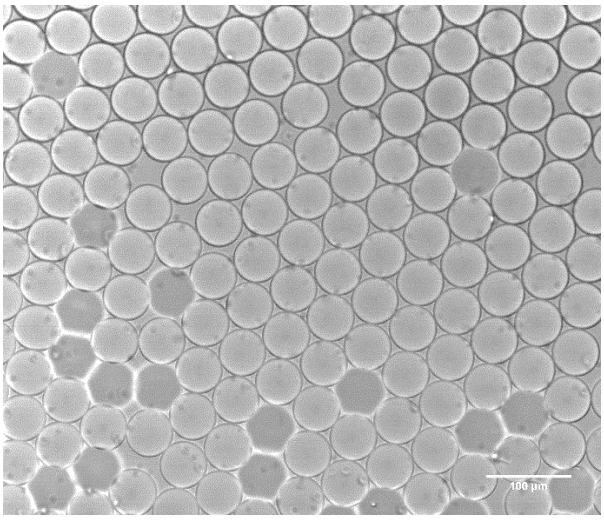

Figure 2: Highly monodisperse water in oil droplets generated with membrane emulsification device, droplet size around 50 µm (droplet size is tunable with nozzle geometry).

Oil-in-water emulsions were produced using a membrane emulsification microfluidic device. The surface of the channel was made hydrophilic. The aqueous continuous phase contains 2 wt. % poly (vinyl alcohol) (PVA, Mw 31,000–50,000, 98%–99% hydrolyzed, Sigma-Aldrich) in DI water and the dispersed phase contains (PLGA, Mw 40,000–75,000, 65:35, Sigma-Aldrich) in dichloromethane (DCM). Oil in water droplets were collected and PLGA microcapsules were ultimately solidified by evaporation of DCM at ambient temperature.

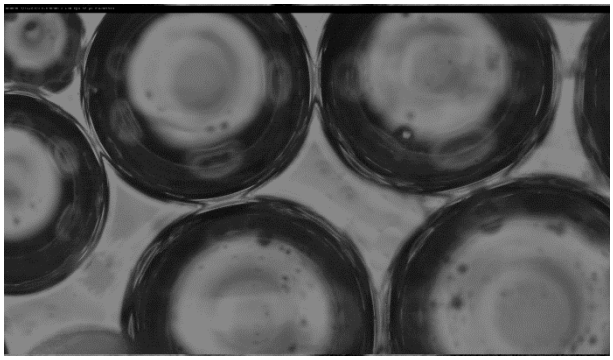

Figure 3: Optical images of monodisperse PLGA encapsulated oil in water emulsion prior to solvent evaporation and conversion to solid PLGA microsphere.

[1] L. Corrêa-Filho, *et al*., "Advances in the Application of Microcapsules as Carriers of Functional Compounds for Food Products." Applied Sciences, vol. 9, no. 3, Sept. 2019, p. 571 doi:10.3390/app9030571.

[2] M.R.I. Shishir, L. Xie, C. Sun, X. Zheng, W. Chen, Advances in micro and nano-encapsulation of bioactivecompounds using biopolymer and lipid-based transporters. Trends Food Sci. Technol. 2018, 78, 34–60.

[3] N. Khalid, *et al*., "Formulation Characteristics of Triacylglycerol Oil-in-Water Emulsions Loaded with Ergocalciferol Using Microchannel Emulsification." RSC Adv., vol. 5, no. 118, 2015, pp. 97151–97162., doi:10.1039/c5ra18354e.