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PRODUCTION OF MICROCAPSULES FOR CONTROLLED FLOW BEHAVIOR IN CONFINED CHANNELS

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Abstract. *The flow of soft particles and microcapsules suspensions through confined spaces is important in many fields, including enhanced oil recovery, reactor feeding, red-blood-cell transport and drug delivery. Biopolymer-based microcapsules are highly hierarchized structures containing an inner phase and a hydrogel shell. In this study, we use a microfluidic device, which combines co-flow and flow-focusing in coaxial glass-capillaries, to produce oil-in-water-in-oil double emulsion templates of gellan microcapsules. Adjusting the fluids flow rates enables the production of microcapsules with a specific diameter and tunable mechanical properties. The effect of these properties on the flow resistance through confined channels is studied by measuring the extra pressure drop associated with the flow of a single microcapsule through a constriction. This research shows how microcapsules can be designed and produced to achieve the desired suspension flow behavior in porous media.*

Keywords: *confined geometry, constriction, pressure drop, flow mobility, targeted delivery*

1. INTRODUCTION

Dynamics of deformable microcapsules in confined flows is relevant for medical, pharmaceutical, food and cosmetic industries. Constricted channels are present in physiological systems and capsules are regarded as adequate models for living cells (Luo et al., 2011, Rorai et al., 2015). Besides that, flooding a dispersion of microcapsules can be an effective enhanced oil recovery method as an alternative to the usually injected emulsions with the advantage of having tunable mechanical properties (Do Nascimento et al., 2017). Capsules can block preferential paths increasing the local pressure in unswept regions which improves mobility ratio and pore scale displacement efficiency in two-phase flow. In addition, capsules can be filled with chemicals, acting as vehicles for targeted delivery in specific areas of the pore space.

Controlling the encapsulation process and release characteristics of the microcapsules is essential for an adequate application of these elements. This ultimately depends on the technique and material chosen to produce the microcapsules. Microfluidics is an effective technique for fabricating monodisperse double emulsion templates that are subsequently converted into microcapsules with well-controlled release properties (Utada et al., 2005). It enables a fine control of the template dimensions and offers high flexibility regarding the materials that can be used to form the microcapsule shell.

Most biodegradable polymers are biocompatible and thus very attractive as shell materials especially when the application involves interaction with living organisms and natural degradation of microcapsules. Gellan gum is a linear, anionic, and high molecular weight exopolysaccharide secreted by the bacterium Sphingomonas elodea that produces biocompatible hydrogels. The structures formed are thermo (Graham et al., 2019) and pHresponsive (Morris et al., 2012).

Some numerical simulations addressing the flow of microcapsules in narrow capillaries can be found in literature (Lefebvre and Barthes-Biesel, 2007) but there are fewer experimental studies. Risso et al. (2006) have experimentally analyzed the flow of capsules flowing in a tube of 4 mm diameter with all capsules being smaller than the diameter of the tube. Leclerc et al. (2012), in turn, studied the flow of microcapsules with diameters greater than the constriction using convergent-divergent square microchannels.

The present paper reports the production of gellan microcapsules from O/W/O double emulsion templates using a glass-capillary microfluidic device as firstly proposed by Utada et al. (2005). We show how the microcapsule diameter and shell thickness can be controlled by adjusting the flow rates of the fluids that compose them. Then, microcapsules are designed and produced to achieve the desired suspension flow behavior in porous media. The effect of microcapsules properties on flow resistance is studied by measuring the extra pressure drop associated with the flow of a single microcapsule through a convergent-divergent tube with a diameter of 100 μm. Several microcapsules were used, including capsules with a diameter higher than the one of the constriction. Results indicate that microcapsule diameter and shell thickness can strongly affect microcapsule response to external stress.

2. METHODOLOGY

2.1 Microcapsule production

Gellan microcapsules are fabricated using a glass microcapillary device described by Michelon et al. (2020). It has two cylindrical capillaries (0.58 mm ID/1 mm OD, World Precision Instruments Inc., USA) axially aligned 75μm apart within a slightly larger square capillary (Atlantic International Technology Inc., USA). The cylindrical capillaries are tapered to an inner diameter of approximately 20μm with a micropipette puller (model P-1000, Sutter Instrument Co., USA). Then, the tip of the injection capillary is sanded to an inner diameter of 50 μm and the tip of the collection one to 250 μm. They are treated for 60 minutes with a polyelectrolytes solution composed of 1 wt.% poly(acrylamide-co-diallydimethyl-ammonium chloride) (Sigma-Aldrich, USA) and 2 mol/L NaCl to render a hydrophilic surface and with a commercial rain repellent Glass Shield (Inove Pack do Brasil, Brazil) to render a hydrophobic surface, respectively.

The inner phase of the microcapsules flows through the injection capillary and the middle phase in the same direction through the interstices between the injection and the square capillaries. The continuous phase, in turn, flows in the opposite direction through the interstices between the collection and square capillaries. Then, all three fluids are forced through the exit orifice of the collection tube as core-shell droplets are generated. The flow rates are controlled by syringe-pumps (model Pump 11, Harvard Apparatus, USA) and an inverted microscope (model DMi8, Leica Microsystem, Germany) equipped with a high-speed camera (model Fastcam SA-3, Photron, USA) is used to monitor the O/W/O template formation. After that, the microcapsules are collected in a glass vial with a small volume of hexane. Immediately after, acetate buffer (0.074 mol/L, pH 4.5) is added to the vial, the hexane excess containing the oil from the continuous phase is removed, and the residual hexane is evaporated at room temperature for 24 hours to ensure an oil-free capsular dispersion.

The microcapsules are made of: a refined commercial sunflower oil (Liza, Cargill Agricola S.A., Brazil) labeled with an orange food-grade dye as inner phase; a mixture of 0.5 wt.% or 1 wt.% low-acyl gellan gum Kelcogel® CG-LA (CP Kelco Brasil S/A, Brazil) and 2 wt.% polyoxyethylene sorbitan monolaurate, Tween® 20 (Sigma-Aldrich, USA), in ultrapure water with resistivity 18.2 MΩ/cm (Direct-Q3 UV System, Millipore Co., USA) as middle phase; and a sunflower oil dispersion containing 1 wt.% calcium acetate (Sigma-Aldrich, USA) and 5 wt.% polyglycerol-polyricinoleate commercially named Grinstead® PGPR super (Danisco Brasil, Brazil) as continuous phase.

2.2 Flow through constriction

A constricted glass capillary with a channel to constriction diameter ratio of 300:100 μm made by Hilgenberg (Germany) was used in the experiments. It was treated with a polyelectrolytes solution composed of 1 wt% poly(acrylamide-codiallydimethyl-ammonium chloride) (Sigma-Aldrich, USA) and 2 mol/L NaCl to render a hydrophilic surface and then it was fixed on a microscope slide with Epoxy® resin (Devcon Corp.,USA).

A Fluigent system was used to feed the suspension through the capillary at constant flow rates and measure the pressure response. It enables the control of the flow rate as well as of the dispense volume once the applied pressure automatically adjusts in the background to maintain the flow rate. An inverted microscope (model DMi8, Leica Microsystem, Germany) equipped with a high-speed camera (model Fastcam SA-3, Photron, USA) and a second computer were used to monitor and record real time images of microcapsules flow.

3. RESULTS

Monodisperse microcapsules can only be formed at a specific flow regime, called dripping at which the breakup of the inner and middle phases occurs simultaneously and at the same position, near the entrance of the collection capillary, and double emulsion is generated with a single inner phase drop. At a fixed value of the inner and outer flow rates, the formation of monodisperse O/W/O templates with a single inner core only occurs inside a certain range of the middle phase flow rate Q_m. Figure 1 presents the operability window as a function of middle and outer phase flow rates at a constant inner phase flow rate Q_i = 100 mL/h. The open symbols represent flow conditions that lead to the desired continuous dripping regime while the filled symbols represent flow conditions that do not lead to the desired dripping regime.

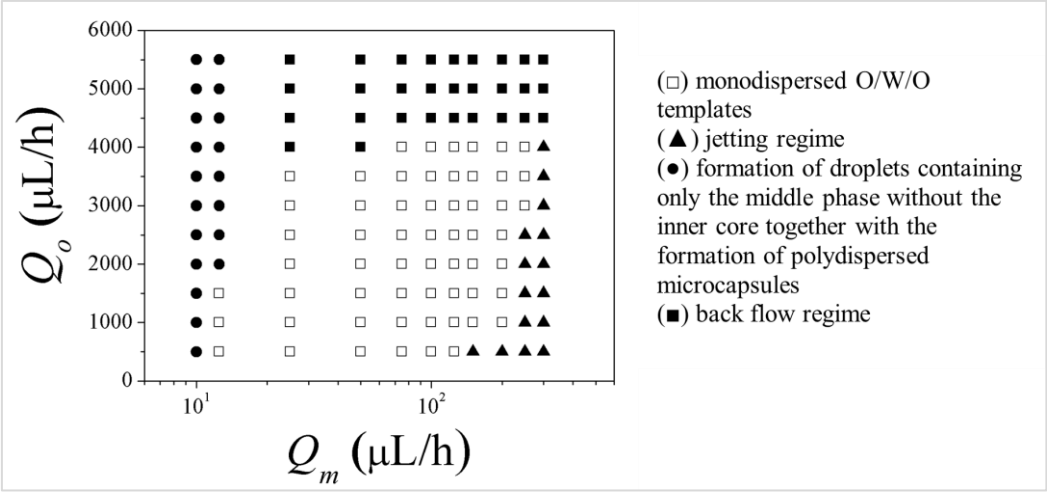

Figure 1. Operability window as a function of the flow rates (Q_m and Q_o) at a fixed Q_i = 100 mL/h.

The effect of the flow rates on the microcapsule diameter and shell thickness is shown in Fig. 2 and Fig. 3, respectively. For the range of parameters explored, microcapsules were produced with a diameter ranging from 95 to 200 mm with a maximum coefficient of variation of 5%.

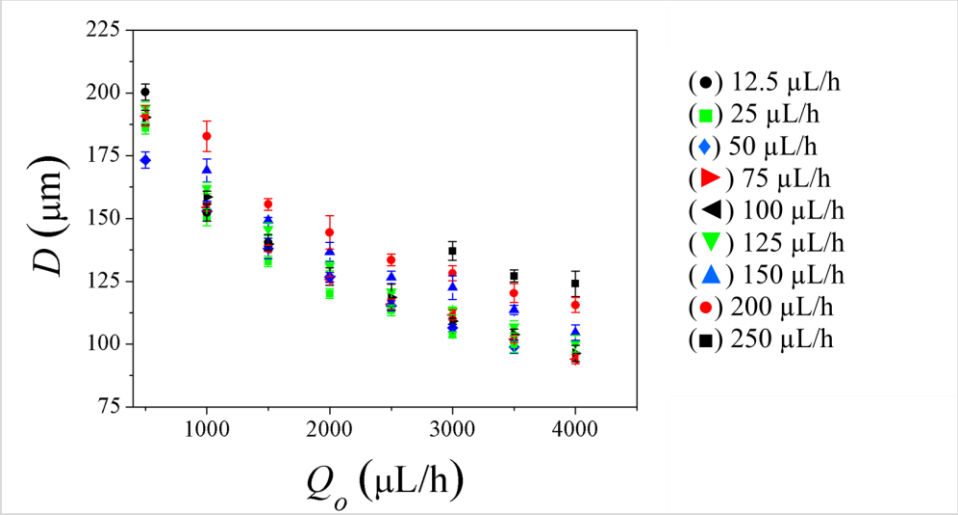

Figure 2. Effect of the flow rates on the microcapsule's diameter (D) for different valued of Q_m.

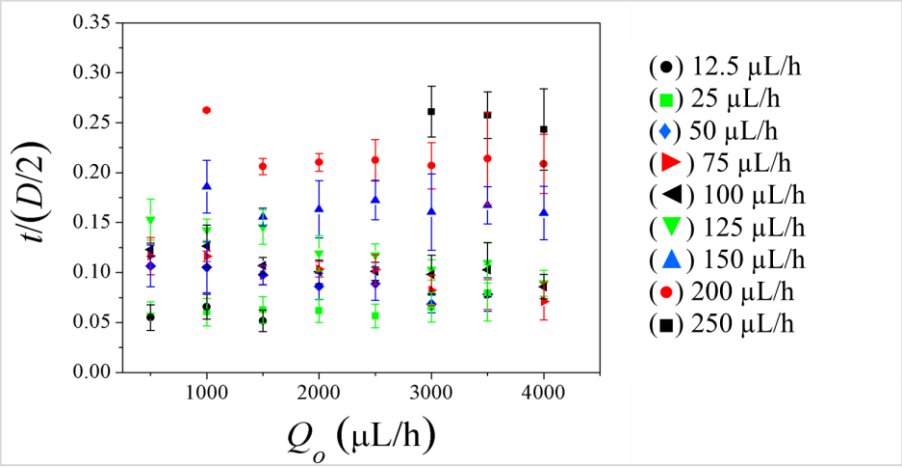

Figure 3. Effect of the flow rates on shell thickness in units of droplet radius for different values of Q_m.

Some of the batches of microcapsules with different mechanical characteristics were selected to be used in the constricted capillary experiments. The effect of the amount of gellan gum in solution to form the shell, the capsule size and the shell thickness on the flow behavior were evaluated. Results were all obtained at a flow rate of 0.2mL/h, which is the minimum required to accurately measure the pressure-drop evolution.

Microcapsules can undergo two types of deformation during the experiments. It can either be a reversible deformation, in which the microcapsule returns to its original shape after flowing through the constriction, or the microcapsule ruptures at a certain level of pressure-drop during its passage. In both cases, it is possible to measure a pressure-drop response based on the difference between the pressure drop measured when the microcapsule (dispersed phase) is in the constriction and the one needed to push only the continuous phase at the same flow rate. Even though it is known that, in the case of rupture, the mobility reduction would be higher if rupture did not occur, all values are reported for comparison purposes.

Figure 4 shows a microcapsule that deforms but does not rupture due to the imposed mechanical strain (reversible deformation). It is possible to see some distortion, but the microcapsule still preserves its membrane integrity, which can be verified by the absence of leakage. After passing through the constriction, the microcapsule recovers its spherical shape. The pressure response during the entire event is showed in Fig. 5. Each moment captured in Fig. 4 (I –V) is associated to a region of the graph in Fig. 5.

Conversely, Fig. 6 shows a microcapsule being ruptured as it is forced through the constriction. Ultimately, the spherical shape is not maintained and the inner content is released to the medium.

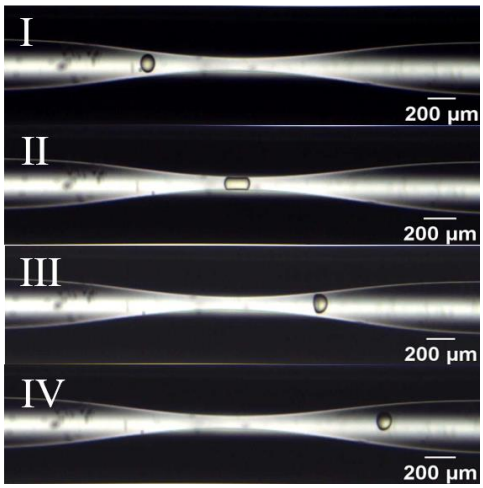

Figure 4. Microcapsule undergoes reversible deformation while passing through the constriction.

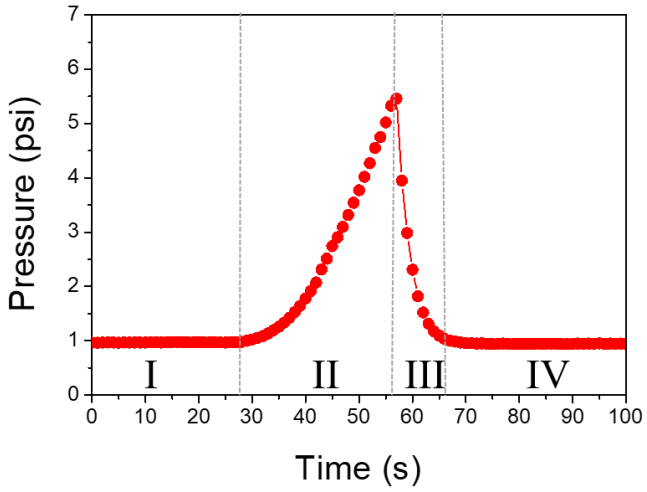

Figure 5. Pressure evolution correspondent to microcapsule undergoing reversible deformation while passing through the constriction.

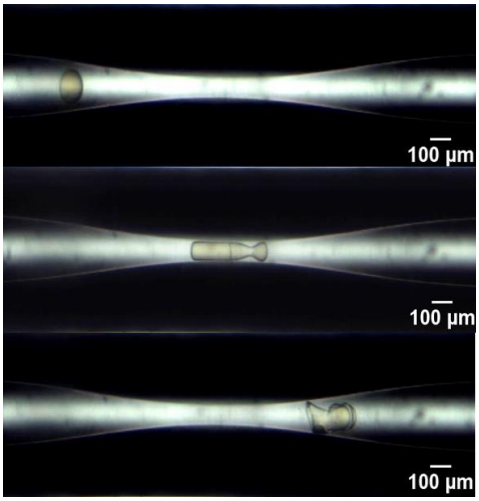

Figure 6. Microcapsule ruptures while passing through the constriction

Table 1 summarizes the averaged maximum pressure-drop and the type of deformation resulted by the flow of each microcapsule batch through the capillary. At least five measurements were made for each batch of capsules. Reversible deformation was only observed in microcapsules from two batches: #5 and #7, despite their differences in size and shell thickness. Figure 7 presents a map on the diameter – shell thickness space of the conditions that led to capsule rupture for 0.5 wt% gellan concentration. The minimum thickness that leads to reversible deformation increases with the level of capsule strain as it flows through the constriction.

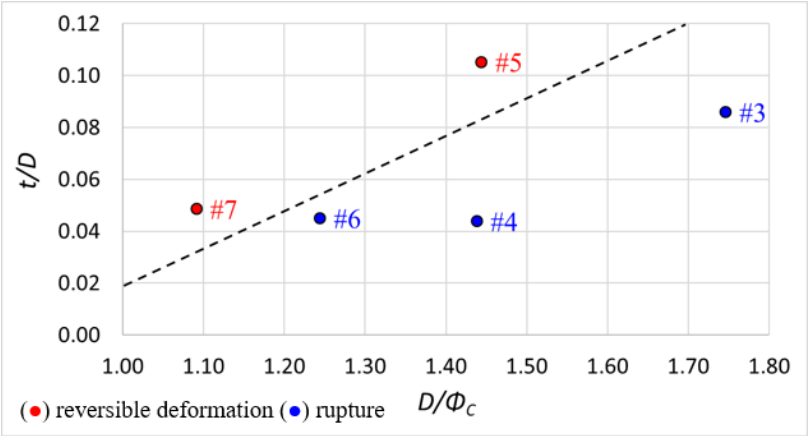

Figure 7. Map of type of deformation as a function of shell thickness to capsule diameter ratio and capsule diameter to constriction diameter ratio.

Table 1. Main properties of the microcapsules used in the experiments, maximum pressure-drop resulted by the flow of each batch of microcapsules through the capillary (ΔP) and type of deformation observed.

Microcapsule	Gellan (%wt)	D (µm)	t (µm)	ΔP (psi)	Deformation
#1	1	174.3 ± 2.1	4.9 ± 0.6	1.81 ± 0.55	rupture
#2	1	175.5 ± 6.1	12.3 ± 1.8	6.19 ± 1.73	rupture
#3	0.5	174.6 ± 4.6	15.0 ± 2.1	6.19 ± 1.10	rupture
#4	0.5	143.8 ± 4.2	6.3 ± 1.5	0.72 ± 0.16	rupture
#5	0.5	144.4 ± 6.7	15.2 ± 3.7	5.04 ± 0.57	reversible
#6	0.5	124.4 ± 1.7	5.6 ± 1.0	< 0.3	rupture
#7	0.5	109.1 ± 2.9	5.3 ± 1.1	< 0.3	reversible

From the outcomes observed when one of the parameters (diameter, shell thickness or gellan concentration) is varied at a time, while the other two are kept constant, it seems that microcapsule diameter and shell thickness can have a strong effect on how a microcapsule respond to the external stress. A more effective effect may be possible when these two parameters are properly combined. On the other hand, for the range explored, gellan concentration does not affect pressure difference, suggesting that the amount of polymer used to form the shell may have a minor effect on the response of microcapsules to external stress.

4. CONCLUSIONS

We successfully produced biopolymer-based microcapsules through a glass-capillary microfluidic device using entirely FDA-approved materials. The operability window of the process was determined as a function of the flow rate of each phase. It is possible to control the shell thickness by fixing the flow rate of the inner phase and varying the flow of the middle phase while a systematic variation in the capsules diameter can be achieved by changing the flow rate of the continuous phase.

Regarding the constriction experiments, conditions at which microcapsules do not rupture were determined. Results show how microcapsules can be designed and produced to achieve the desired suspension flow behavior in confined spaces. This study indicates the adequate mechanical properties that a microcapsule should be produced with to have the response required by a specific application. Microcapsules that present reversible deformation when flowing through the constriction are suitable for flow mobility control while the ones that rupture when passing through the constriction may be used for controlled delivery triggered by external stress.

5. ACKNOWLEDGEMENTS

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