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PDMS MICROCAPSULES FOR TRIGGERED RELEASE BY OSMOTIC PRESSURE

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Abstract. *Monodispersed microcapsules can be produced from double emulsions templates and can be used as vehicles for triggered release in different applications. In the present work, microcapsules with a polydimethylsiloxane (PDMS) shell were produced using a microfluidic device, which combines co-flow and flow-focusing in coaxial glass-capillaries. For the controlled release, osmotic pressure was used as trigger. The PDMS microcapsules were placed in mediums with different osmolality and they were monitored using a confocal microscope. Confocal laser scanning microscopy allows the 3D reconstructions of the capsules to quantify their volume, as well as to determine the capsule's shape. The results point that when the microcapsules are exposed to a hypotonic medium, they swell; whereas, when they are suspended in a hypertonic medium, they shrink and the shell eventually buckles. This work shows that osmolality can work as a trigger for content release and that the dynamics of the release process can be controlled by the osmolality of the medium and capsule properties. This information can be helpful for the use of PDMS microcapsules delivering active compounds for a broad range of applications.*

Keywords: *microfluidics; microcapsules; controlled release; osmotic pressure.*

1. INTRODUCTION

Microcapsules can be used as a vehicle for triggered release in many different applications, such as drug delivery, reactor feeding and oil recovery (Abbaspourrad et al. 2013; Abbaspourrad, Datta, and Weitz 2013; Datta et al. 2014; Michelon, Leopércio, and Carvalho 2020; Zhang et al. 2017). Depending on the application, the microcapsules need to be produced with specific properties considering the trigger mechanism used, so that their content is released at the desired time or location. The precise determination of the dynamics of the release process is critical to guarantee a reliable application of the technique.

The triggering mechanism can be temperature, pH or external stress, for example. In these cases, the release of the active compound occurs when the trigger causes a mechanical rupture of the cross-link cleavage or depolymerization of the shell. Another way to trigger the release of the inner phase is to use osmotic pressure to induce physical changes in the shell. This is an attractive alternative because it works simply adding or removing water to the surrounding environment. Due to the osmotic pressure difference across the shell, the water diffuses to or from the inner phase, resulting in the swelling or the buckling of the microcapsule, respectively.

The technique to fabricate water-in-oil-in-water (W/O/W) double emulsion microcapsules uses the same experimental procedure of Utada et al. 2005 and Do Nascimento et al. 2017, based on the controlled flow inside a glass capillary device. However, in the present work, the osmolality of the inner phase was varied up to values higher than 2000 mOsmol/kg.

We measured the swelling and buckling of polydimethylsiloxane (PDMS) microcapsules when exposed to hypotonic and hypertonic media. To visualize the volume changes, a confocal laser scanning microscope was used. It precisely captures the volume and the shape of each capsule when placed in hypotonic and hypertonic media with different osmolalities. The 3D images produced were later processed and allowed the quantification of the time evolution of swelling and buckling. The results point out that it is possible to control the releasing mechanism using different osmotic and shell properties. Microcapsules flow through confined spaces is an important topic for several biomedical and industrial applications such as enhanced oil recovery (EOR); this brings our research to the future technology innovation.

2. MATERIALS AND METHODS

2.1 Microcapsules production

In order to produce monodispersed microcapsules from a W/O/W double emulsion template, a microfluidic technique was applied. Figure 1 shows a sketch and a real image of the production of microcapsules, composed by two cylindrical glass capillaries with different tip sizes that are coaxially aligned within a square capillary.

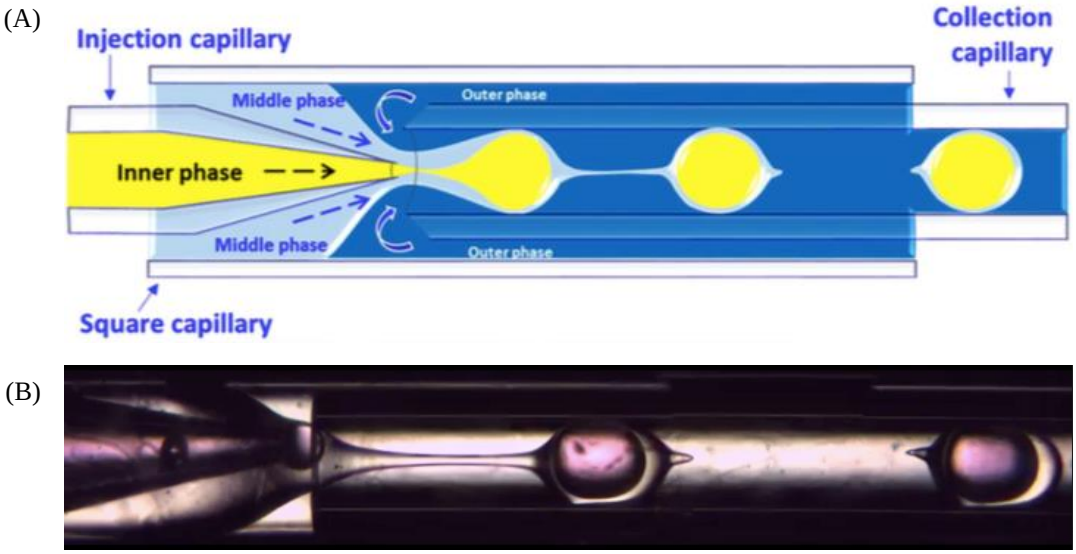

Figure 1. Production of PDMS microcapsules: (A) Sketch of geometry and flow used to produce PMDS microcapsules (available from: Do Nascimento et al. 2017). (B) Image of double emulsion production process. The action of the outer phase causes the middle phase breakup and consequently, drop formation.

The inner phase of the microcapsules consists of pure water or a solution of water and salts, depending on the experiment, mixed with a fluorescent dye (M9140- Methylene Blue by Sigma Aldrich). The elastomer polydimethylsiloxane (PDMS) with a specific fluorescent dye (Oil-Glo 22-P by Spectroline) is used as middle oil phase, injected between the injection capillary and the square capillary. The fluorescent dye allows us to observe and track the behavior of the microcapsules during the controlled release experiments. The outer phase is composed by 10% of poly (vinyl alcohol) (PVA), that is injected from the opposite capillary. PVA is used as polymeric surfactant that provides interface stability, acting as an excellent film former. So, it increases the impermeability of the microcapsules even during the storage and between wash experiments, guaranteeing a residual surface film without hindering the osmotic changes that trigger the capsule's swelling or buckling. In the fabrication process, controlling the flow rate of the middle phase is an important step to produce microcapsules as thin as possible. This is desirable because thin shells are probably easier to break.

Microcapsules were formed with an average diameter of 600 µm, approximately, and with a shell thickness of 10 µm. They were collected in a vial filled with the same fluid that forms their inner phase to provide an isotonic and stable medium for storage before being used in experiments.

2.2 Experiments

Two different experiments were performed: hypertonic tests and the hypotonic tests. To simplify the experimental setup, we designed and used a 3D printer to manufacture a device to hold multiple cavities on the confocal microscope stage. In each cavity the microcapsules were placed in a solution with a different osmolality. The sample holder is shown in Figure 2.

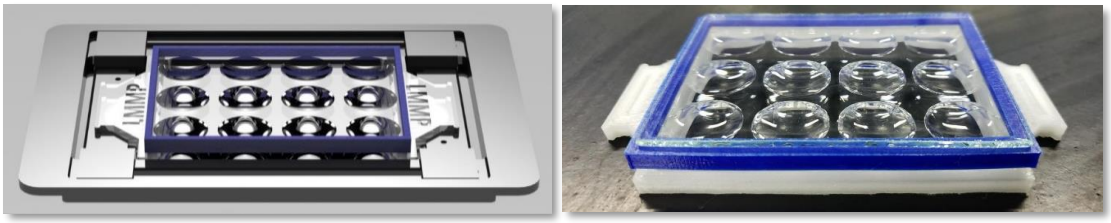

Figure 2. Device created to perform the experiments on confocal microscope. On the left is the model developed in SolidWorks software and on the right-hand side is the final sample holder ready for experiment.

Hypertonic tests

Microcapsules for the hypertonic tests have Milli-Q water with Methylene Blue as inner phase; PDMS in a ratio of 10:1 dyed with Oil-Glo 22 as middle phase; and 10% PVA as outer phase. After production, they were placed in a vial containing Milli-Q water (55 mOsmol/kg) to set an isotonic medium and refrigerated.

In hypertonic experiments, microcapsules were placed in 5 cavities of the device with mediums with different values of osmolality, controlled by the amount of salt added to solution. The values measured were: 55 mOsmol/kg (for control), 103 9mOsmol/kg, 1572 mOsmol/kg, 3209 mOsmol/kg and 3852 mOsmol/kg.

Hypotonic tests

To perform the experiments in hypotonic medium, we used a solution of water and salts with osmolality of 2092 mOsmol/kg with Methylene Blue as inner phase; PDMS in a ratio of 10:1 dyed with fluorescein as middle phase; and 10% PVA as outer phase. After production they were collected in a vial filled with a solution of 2139 mOsmol/kg of osmolality to set an isotonic medium and refrigerated.

Hypotonic experiments were also carried out by submitting microcapsules to environments with 5 different osmolality values: 2139 mOsmol/kg (for control), 1654 mOsmol/kg, 1173 mOsmol/kg, 705 mOsmol/kg and 263 mOsmol/kg.

2.3 Image acquisition and processing

A Leica TCS SP8 confocal laser scanning microscopy (CLSM) was used for visualization of the microcapsules during the experiments. The major advantage of using confocal microscopy is that it allows to reconstruct the 3D image of microcapsules for later volume quantification. This 3D image is composed by a stack of approximately 60 plane images, in which only the fluorescent parts are visible.

The process of image reconstruction is illustrated in Figure 3.

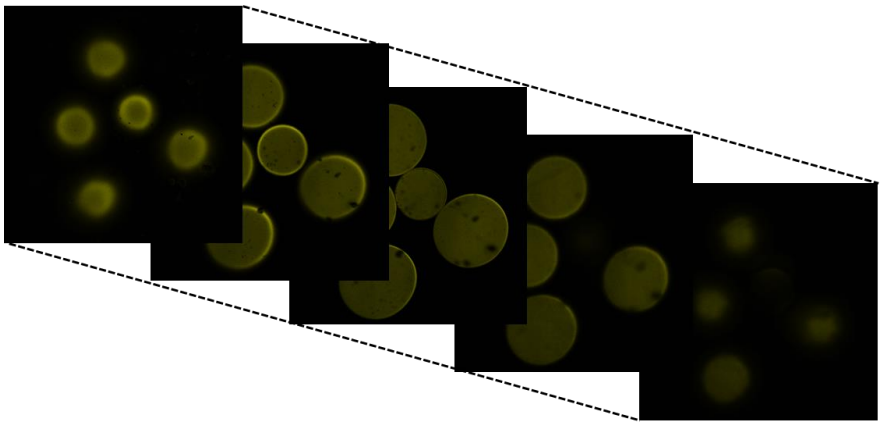

Figure 3. Image stack for 3D reconstruction using CLSM.

The images were obtained using the resonant scanning method that provide an acquisition speed of 12000 hz. The lens used were N-Plan 5x/0.12 Dry for the hypertonic experiment and HC PL Fluotar 5x/0.15 Dry for the hypotonic. The microscope was set to obtain 512x512 px images, with a pixel resolution of approximately 2.3 µm/px. The distance between stacks was 26.8 µm/slice for the hypertonic test and 17.1µm/slice for the hypotonic test.

The volumetric quantification was performed using the ImageJ software. Each image stack was individually processed. To increase the accuracy of the measurement, “close” and “fill holes” operations were applied before the 3D Objects Counter. The 3D Objects Counter tool use the voxels reconstructed from the image stack to generate the volume, surface area, mean distance to surface and other parameters. In this work, only the volume measurement is reported.

3. RESULTS AND DISCUSSION

Hypertonic tests

Figure 4 shows the results obtained in the confocal microscope for the hypertonic tests. The acquisition was performed along 10 hours, with acquisition intervals of 2 hours and 30 minutes. The results show that the microcapsules shrink and the shell buckles. Also, after 10 hours, we can see that a minimum amount of content inside the microcapsule was reached.

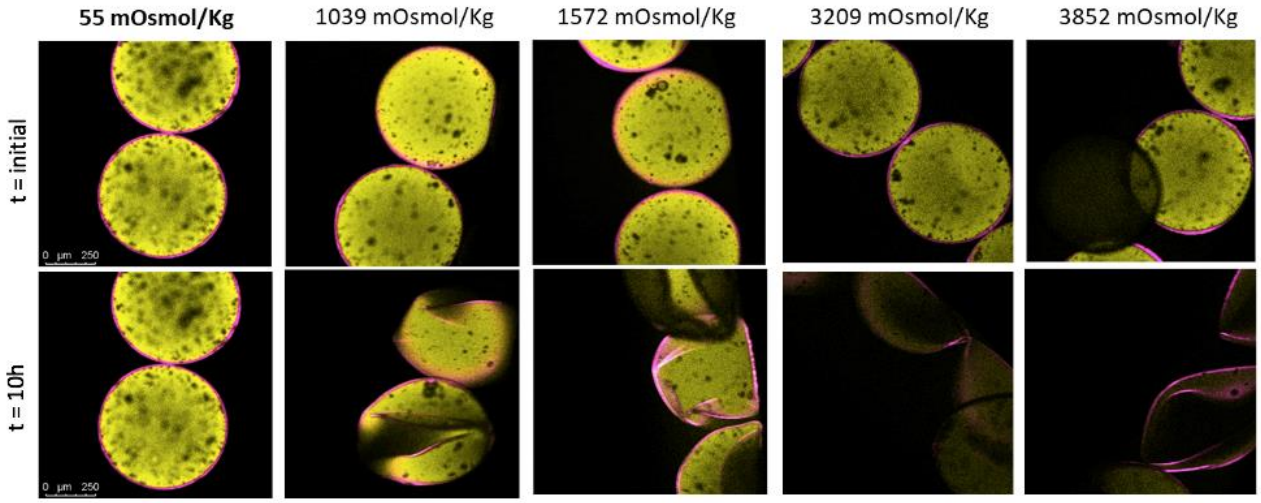

Figure 4. Microcapsules images of hypertonic test. Behavior at the beginning of the immersion and 10h later. The picture for the 55 mOsmol/kg is the control group in which no change was observed.

Through Fig. 4 we can conclude that the microcapsules lost their content over time and depending on the medium of exposure. The higher the osmolality value of the exposure medium is, the greater is the loss of inner content.

Figure 5 shows the variation of volume through time of microcapsules in mediums with different osmolalities. The volume of the inner phase decreases over time in all cases. Besides that, experiments indicate that microcapsules in environments with higher osmolality values present greater loss of inner content.

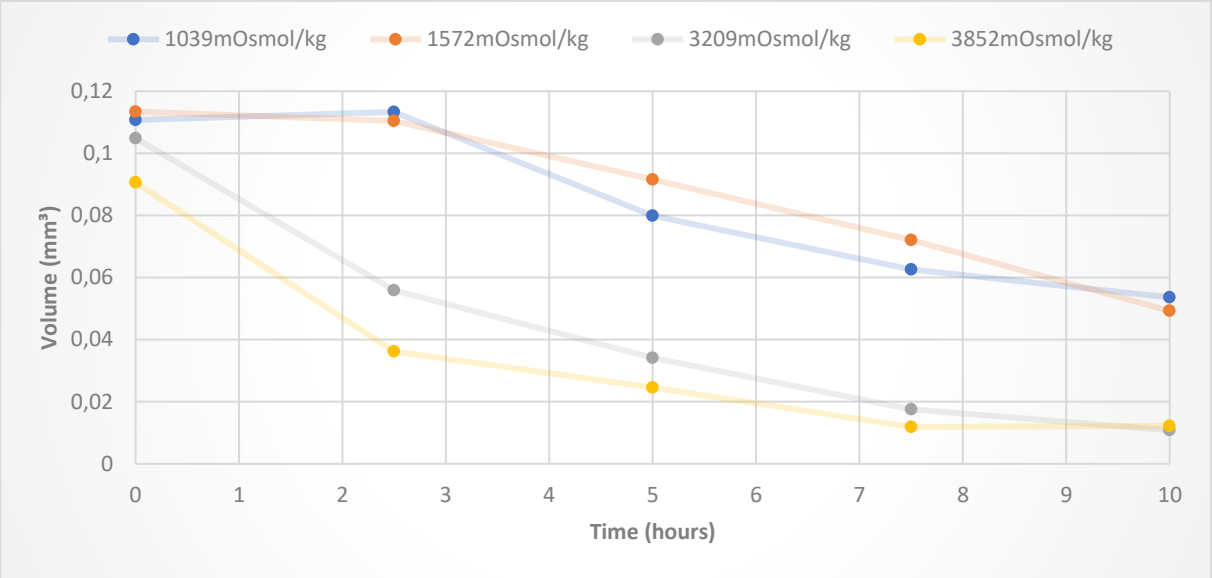

Figure 5. Microcapsules volume as a function of exposure time in hours for the hypertonic test.

Analyzing the plot in Fig. 5, we see that microcapsules exposed to the 1039 mOsmol/kg medium (blue curve) lost 52% of their content after ten hours of exposure, while the ones exposed to a medium of 1572 mOsmol /kg (orange curve) lost 57% of their content. When the medium osmolality was increased to 3209 mOsmol/kg and 3852 mOsmol/kg (gray and yellow curves), the loss substantially increased to 90% and 87%, respectively. The non-linearity of test curves can be justified by the small number of capsules used. The results showed an almost total loss of content for microcapsules immersed in high concentrations of salt which indicates a promising tendency for larger samples.

Hypotonic tests

Microcapsules that underwent hypotonic tests show similar behaviors for different osmolalities: there is a constant swell, that is more pronounced when the osmolality of the medium is smaller.

Figure 6 shows the hypotonic test results obtained in the confocal microscope for the microcapsules exposed to a medium of 263 mOsmol/kg, that is the minimum concentration used in these tests. Although a large swell was observed, even after 7 days of exposure, microcapsules bursting was not observed. This suggests that the PDMS is too elastic and probably only microcapsules with an inner content with osmolality higher than 2139 mOsmol/kg would burst.

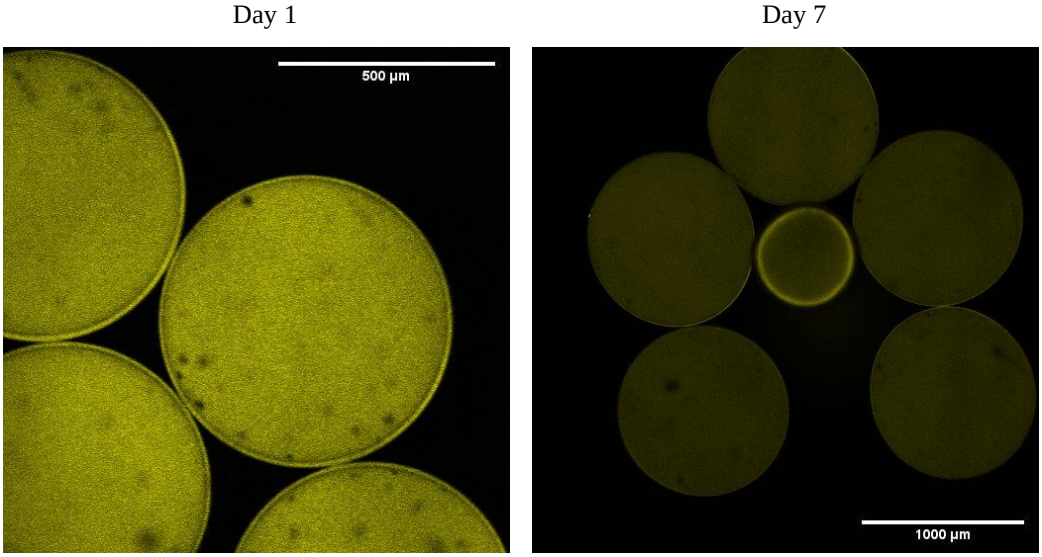

Figure 6. Microcapsules with osmolality of 2139 mOsmol/kg exposed to a medium of 263 mOsmol/kg, at day 1 and day 10 for the hypotonic test.

Figure 7 shows that the volume of the inner phase was increased over time in all cases which is in accordance with microcapsules swelling. Besides that, experiments indicate that microcapsules in environments with lower osmolality values present greater volume variations.

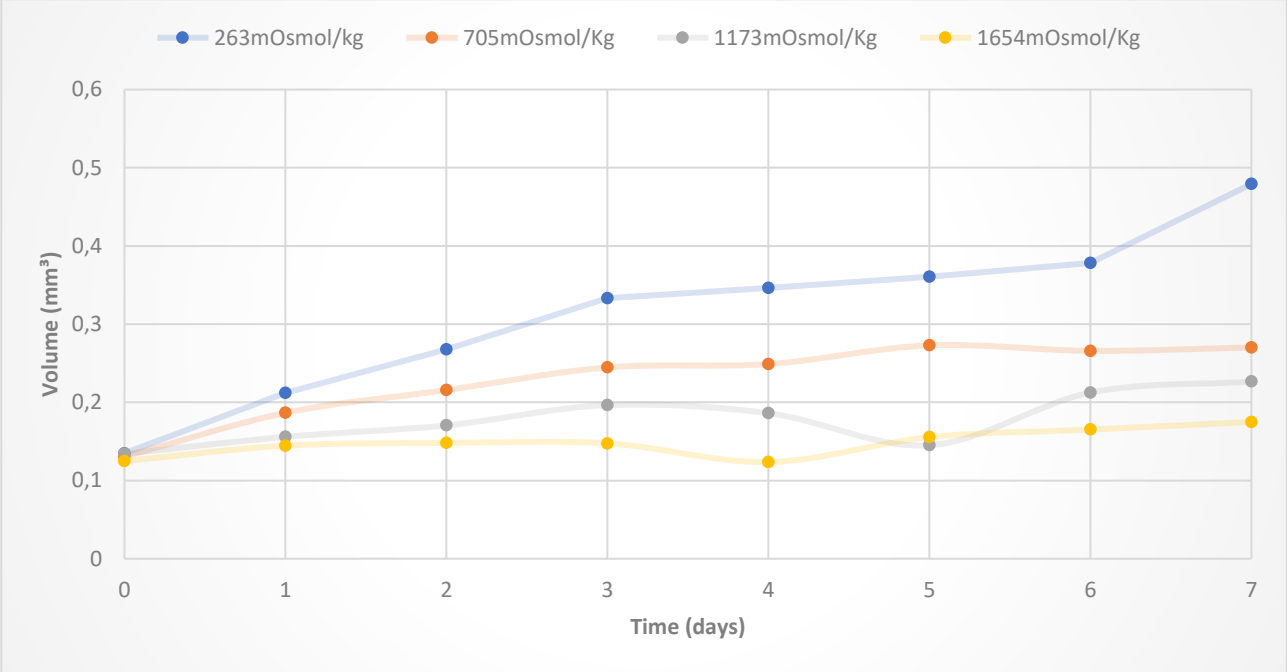

Figure 7. Microcapsules volume as a function of exposure time in days for the hypotonic test.

The plot in Fig.7 shows a smooth swelling of microcapsules when exposed to mediums with osmolality values of 1654 mOsmol/kg (yellow curve) and 1173 mOsmol/kg (gray curve), with volume increase of 29% and 41%, respectively. The increase is even higher (52% and 72%, respectively) for the mediums with lower osmolality: 705 mOsmol/kg (orange curve) and 263 mOsmol/kg (blue curve). So, the mediums with lower salinities are associated to the higher increases of microcapsules volume.

4. CONCLUSIONS

We have used microfluidics to prepare PDMS microcapsules with different amounts of salt in the inner content for controllable release triggered by osmotic pressure. This was achieved by submitting the microcapsules to hypotonic and hypertonic mediums while tracking their volume variations using confocal microscopy. We successfully demonstrated that it is possible to trigger the inner content release of PDMS microcapsules with osmotic pressure by exposing them to a medium with solute concentration approximately 3.5 times higher than the inner phase solute concentration.

5. ACKNOWLEDGEMENTS

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6. REFERENCES

Abbaspourrad, Alireza, Nick J. Carroll, Shin Hyun Kim, and David A. Weitz. 2013. “Polymer Microcapsules with Programmable Active Release.” *Journal of the American Chemical Society* 135(20): 7744–50.

Abbaspourrad, Alireza, Sujit S. Datta, and David A. Weitz. 2013. “Controlling Release from PH-Responsive Microcapsules.” *Langmuir* 29(41): 12697–702.

Datta, Sujit S. et al. 2014. “25th Anniversary Article: Double Emulsion Templated Solid Microcapsules: Mechanics and Controlled Release.” *Advanced Materials* 26(14): 2205–18.

Michelon, Mariano, Bruna C. Leopércio, and Marcio S. Carvalho. 2020. “Microfluidic Production of Aqueous Suspensions of Gellan-Based Microcapsules Containing Hydrophobic Compounds.” *Chemical Engineering Science* 211: 115314. https://doi.org/10.1016/j.ces.2019.115314.

Do Nascimento, Débora F. et al. 2017. "Flow of Tunable Elastic Microcapsules through Constrictions." *Scientific Reports* 7(1): 1–7.

Utada, Author A S et al. 2005. "Monodisperse Double Emulsions Generated from a Microcapillary Device Published by : American Association for the Advancement of Science Stable URL : Http://Www.Jstor.Org/Stable/3841301 REFERENCES Linked References Are Available on JSTOR for This Article :" 5721(5721): 537–41.

Zhang, Weixia et al. 2017. "Osmotic Pressure Triggered Rapid Release of Encapsulated Enzymes with Enhanced Activity." *Advanced Functional Materials* 27(29): 1–7.

7. RESPONSIBILITY NOTICE

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