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Abstract

This thesis presents the production of macroporous polymer particles by polymerisation of multiple high internal phase (ratio) emulsion (HIPE) templates and their potential use as delivery systems for encapsulated active ingredients. Beads with a closed surface and interconnected or close celled internal pore structure are attractive as delivery systems of active ingredients for a wide range of applications, such as in the Oil & Gas industry or personal care applications. To optimise the encapsulation efficiency and to allow for controlled release of the encapsulated active ingredients, control of the bead surface and internal pore structure is necessary.

The first part of this thesis explores different routes to control the internal pore structure and the outer surface of beads produced by sedimentation photopolymerisation. Through emulsion engineering, the internal pore structure of macroporous poly(merised) (MMA-co-EGDMA) HIPE beads was modified to produce beads with an interconnected or close celled pore structure. Moreover, by changing the locus of initiation and adding different components to the secondary aqueous phase used as external phase, the surface interconnectivity of polyHIPE beads was modified.

The second part of the thesis focuses on the production of macroporous beads. In order to address two known problems in the synthesis of polyHIPE beads by microfluidic polymerisation; i) the frequent clogging of the microfluidic setup and ii) the low production rates. A novel scalable synthesis method, which we called macrofluidic polymerisation, was developed. In this method, a macrofluidic tubular plug flow reactor was used to polymerise W_1/O emulsion template droplets after injection into a flowing secondary carrier phase (W_2). The bead size was controlled by adjusting the emulsion injection and carrier phase flow rates. A maximum emulsion injection flow rate of 54 mL/l could be used avoiding clogging, even when with high internal phase emulsion templates and high surfactant concentrations were used.

In order to demonstrate the possibility to encapsulate an active ingredient in polyHIPE beads, emulsion templates containing an aqueous HCl solution as dispersed phase (W_1) were used to synthesise macroporous beads by macrofluidic polymerisation. After polymerisation of the minority organic phase, the active ingredient was encapsulated in the internal pore structure of the beads. It was shown that 144 $\mu\text{mol/g}$ of HCl could be encapsulated in the macroporous polymer beads produced using the macrofluidic polymerisation method, representing an encapsulation efficiency of 49 %. In order to further increase the encapsulation efficiency, macroporous beads were produced by multi-drop polymerisation. Here, emulsion droplets were printed onto and so suspended from a titanium mesh and photopolymerised. Using this method, an encapsulation efficiency of the model active ingredient HCl of 95 % was reached.

Zusammenfassung

Diese Doktorarbeit stellt die Produktion von makroporösen Polymerpartikeln durch die Polymerisation mehrerer Emulsionsvorlagen (HIPE) mit hoher innerer Phase (Ratio) und ihre mögliche Verwendung als Abgabesysteme für aktive verkapselte Inhaltsstoffe vor. Kügelchen mit einer geschlossenen Oberfläche und einer miteinander verbundenen oder engzelligen inneren Porenstruktur sind als Abgabesysteme von aktiven Bestandteilen für eine breite Palette von Anwendungen attraktiv, wie beispielsweise in der Öl- und Gasindustrie oder in Körperpflegeanwendungen. Um die Einkapselungseffizienz zu optimieren und eine kontrollierte Freisetzung der eingekapselten Wirkstoffe zu ermöglichen, ist eine Kontrolle der Kügelchenoberfläche und der inneren Porenstruktur notwendig.

Der erste Teil dieser Arbeit untersucht verschiedene Wege zur Kontrolle der inneren Porenstruktur und der äußeren Oberfläche von Kügelchen, die durch Sedimentationsphotopolymerisation hergestellt werden. Durch technische Weiterentwicklung der Emulsion wurde die innere Porenstruktur von makroporösen polymerisierten (MMA-co-EGDMA) HIPE-Kügelchen modifiziert, um Kügelchen mit einer miteinander verbundenen oder engzelligen Porenstruktur herzustellen. Darüber hinaus wurde die Oberflächenbindungsfähigkeit von PolyHIPE-Kügelchen verändert, indem der Initiationsort geändert und verschiedene Komponenten der als äußere Phase verwendeten sekundären wässrigen Phase hinzugefügt wurden.

Der zweite Teil der Arbeit konzentriert sich auf die Herstellung von makroporösen Kügelchen. Um zwei bekannte Probleme bei der Synthese von PolyHIPE-Kügelchen durch mikrofluidische Polymerisation anzugehen; i) das häufige Verstopfen des mikrofluidischen Aufbaus und ii) die niedrigen Produktionsraten. Eine neuartige, skalierbare Synthesemethode, die wir als makrofluidische Polymerisation bezeichneten, wurde entwickelt. Bei diesem Verfahren wurde ein Makrofluid-Röhren-Strömungsreaktor verwendet, um W 1/ O Emulsion Vorlagetröpfchen nach Injektion in eine fließende sekundäre Trägerphase (W2) zu polymerisieren. Die Kugelgröße wurde durch Einstellung der Emulsionsinjektions- und

Trägerphasenströmungsraten gesteuert. Eine maximale Emulsionsinjektionsflussrate von 54 ml/l könnte verwendet werden, um ein Verstopfen zu vermeiden, selbst wenn Emulsionsvorlagen mit einer hohen inneren Phase und hohe Tensidkonzentrationen verwendet wurden.

Um die Möglichkeit zu demonstrieren, einen Wirkstoff in PolyHIPE-Kügelchen einzukapseln, wurden Emulsionsmatrizen mit einer wässrigen HCl-Lösung als dispergierte Phase (W1) verwendet, um makroporöse Kügelchen durch makrofluidische Polymerisation zu synthetisieren. Nach der Polymerisation der organischen Minoritätsphase wurde der Wirkstoff in die innere Porenstruktur der Kugeln eingekapselt. Es wurde gezeigt, dass 144 $\mu\text{mol/g}$ HCl in den makroporösen Polymerkügelchen, die unter Verwendung des makrofluidischen Polymerisationsverfahrens hergestellt wurden, eingekapselt werden können, was eine Einkapselungseffizienz von 49 % darstellt. Um die Verkapselungseffizienz weiter zu erhöhen, wurden makroporöse Perlen durch Mehrtropfenpolymerisation hergestellt. Hier wurden Emulsionströpfchen auf ein Titannetz gedruckt und so aufgehängt und photopolymerisiert. Mit dieser Methode wurde eine Verkapselungseffizienz des Modellwirkstoffes HCl von 95 % erreicht.

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Chapter 1. Aims and outline

1.1 Introduction

New legislation in the USA and several other countries, including the European Union aims to regulate hydraulic fracturing, commonly known as fracking. These regulations aim to control and reduce the amounts of chemicals used to make the process safer from an environmental point of view.¹⁻² Besides large amounts of water, which is the major component used in fracking, this specific sector of the Oil & Gas industry utilises a wide variety of active ingredients as additives.³ In order to enhance rock permeability various acids that react with the rock components are used along with corrosion inhibitors, such as alcohols, glycols, organic acids or polymers to protect the steel pipes and equipment. Furthermore, additives such as friction/drag reducing agents (typically high molecular weight polymers), gelling agents (guar gum or hydroxyethyl cellulose), and biocides (gluteraldehyde or sodium hydroxide) among others are used.⁴ Different acids are utilized in a technique called acidizing, which is common practice used to enhance the extraction of oil and gas from shale rock.⁵ It involves pumping from a few hundreds to several thousand litres of an acid down a well to dissolve the rock formations increasing the accessibility to the resources. The aqueous acids normally used in acidizing are hydrochloric acid, sulfuric acid, perchloric acid, nitric acid and acetic acid depending on the well characteristics in concentrations ranging from about 3 % to about 28 % or more by weight of the total fracture acidizing fluid.⁶ The acid type and concentration used is selected based on the minerals that compose the rock formation (commonly limestone and dolomite). After a number of hours, the solution is brought back up to the surface as wastewater. But hydraulic fracturing not only produces flowback of fracking fluids but also formation water, a water based solution that as the name suggest flows back to surface during and after the completion of hydraulic fracturing. Depending on the well conditions, the total volumes of wastewater returning to the surface may vary between 10% to 80 % of the originally injected volumes.⁷ All these fluids are considered to be wastewater. Handling the large amounts of wastewater produced can be challenging, while an estimated of 70 % can be reused through recycling,⁸ injection into deep disposal wells and treatment and disposal into watercourses are commonly used disposal alternatives.⁹ Many of these disposal

options are related to environmental¹⁰ or geological¹¹ risks or may not be available or allowed.¹²

Encapsulation of different active ingredients in porous polymer beads that allow for controlled release provide an efficient alternative to precisely deliver an active ingredient needed to the desired location. Porous polymer beads are spherical polymer particles with an interconnected or closed pore structure (Figure 1-1).

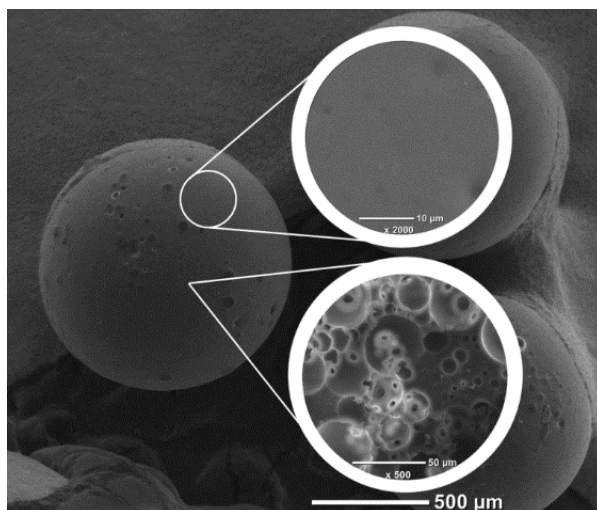


Figure 1-1. Macroporous bead with an interconnected pore structure and closed surface

Beads filled with different acids to degrade debris from the drilling stage or increase permeability of the rock formations, glutaraldehyde used as biocide, enzymes to degrade guar gum to modify its viscosity or other reactive ingredients could be used in fracking fluids to deliver such substances deep underground. Thus, reducing the total amount of chemicals needed and the risk of spillage and contamination.

Besides their potential application as delivery system in the Oil & Gas industry, porous polymer beads containing active ingredients might be useful in several fields.¹³ For instance, beads with encapsulated self-healing agents can be used in composite materials to prevent fracture growth and structural failure.¹⁴ Porous polymer beads are also used in separation science, ion-exchange columns, blood plasma detoxification,¹⁵ and as macroporous supports for cell culture,¹⁶ enzymes¹⁷ and catalyst.¹⁸ However, most of these applications require an interconnected pore structure and high surface areas.

The production of macroporous polymer beads from multiple emulsion templates is a flexible and convenient approach. This is due to the possibility to tailor the bead size and their final internal pore structure and the surface porosity by adjusting the emulsion composition and

emulsification conditions. But the use of emulsion templating is limited by the thermodynamic instability of such systems and their complex structure. It is necessary to understand several parameters of the emulsion behaviour, such as stability over time, temperature sensitivity and rheological properties to name a few, before it can be used for large production of macroporous micrometre or millimetre sized polymer beads.

The synthesis of porous polymer beads from multiple emulsion templates can be realised by several techniques. The combination of multiple emulsion templating and microfluidic devices is one of the most recently developed approaches to produce macroporous polymer beads.¹⁹ In this case, an emulsion is injected into an appropriate tertiary flow forming droplets with controlled size and extremely low size dispersions. After injection, the continuous phase of the emulsion droplets is quickly photopolymerised leading to solid macroporous beads. However, the use of microfluidic devices to produce multiple emulsion droplets also has its limitations. To operate in a region of low turbulence (laminar flow) that allows control over bead size low flow rates are needed, which leads to poor production rates. In order to increase the production capacity, an alternative is the use of several microfluidic devices working in parallel.²⁰ But parallelization entails an increase in the complexity and cost of the microfluidic devices.

The production of beads with porosities above 75 % requires the use of emulsion templates with a similar content of dispersed phase, these emulsions are known as High Internal Phase Emulsion (HIPEs). A usual characteristic of HIPEs is their high viscosity this however results often in clogging of the microfluidic devices used for the production of macroporous beads. These drawbacks, a common feature of microfluidic devices and for simple setups based on commercial tubing and needles, are solved by replacing the entire tubing. In case of more complex microfluidic devices, such as glass capillaries or polydimethylsiloxane (PDMS) devices, unclogging and cleaning can be even more complicated. Often, clogging of the microfluidic device forces to discard the entire setup or disassemble a delicate structure to clean the interior. Both options are time consuming and involve an economic cost, dismantling the setup requires previous expertise in the handling.

1.2 Aim and objectives of the work

The motivation of this work is to find a simple alternative for the production of rather large volumes of macroporous polymer beads compared to current microfluidic devices. In order to

meet the requirements of the applications previously mentioned, beads with an average size between 200 – 1000 μm and controlled size distribution are desired.

The main application in mind for such beads is their use as delivery system for active ingredients. Therefore, the beads should be able to encapsulate a model active ingredient used in the Oil & Gas industry. Due to the complexity of the variables governing the emulsion templating technique, along with the encapsulation and release process, a better understanding of the properties of the emulsion templates and the resulting bead morphology is necessary (see Chapters 4 and 5).

The aim is to create beads with a closed or interconnected cell structure and a closed surface and, therefore, to achieve a better control of the active ingredient release under different conditions and requirements. Furthermore, due to the various applications available for porous beads with an open surface, the possibility to create beads with a controlled pore surface is explored.

Based on previous work in our research group and the literature, an emulsion formulation based in methy methacrylate (MMA) and ethylene glycol dimethacrylate (EGDMA) as organic phase was chosen. This particular combination of monomer and crosslinker allowed the synthesis of porous materials with enhanced mechanical properties.²¹ This characteristic is required to handle the demanding conditions typical of Oil & Gas drilling environments.

Therefore, the objectives of this is doctoral work are:

1. Develop a scalable method to produce macroporous beads with controllable size and size distribution with higher production rates as compared to a typical microfluidic approach.
2. Encapsulate a model active ingredient typical for the Oil & Gas industry (HCl) in the dispersed phase of a polymerisable emulsion and produce solid beads loaded with the active ingredient from multiple emulsion templates.
3. Identify formulation and synthesis alternatives in order to tailor the internal and surface morphology of the produced beads, and therefore, achieve a better control over the release rate and encapsulation efficiency of the active ingredients.

1.3 Structure of the thesis

In **Chapter 2**, a detailed theoretical background of emulsions including stability, emulsifiers and emulsion rheology is provided to the reader. Later, the use of emulsion templating as route to obtain macroporous polymers is reviewed including different alternatives to tailor morphology and mechanical properties. Additionally, the relevant literature and recent advances in the production of macroporous beads through emulsion templating are discussed. Furthermore, the encapsulation of active ingredients, especially HCl, into multiple emulsion systems and later macroporous beads is reviewed.

The experimental methodology used in this thesis is detailed in **Chapter 3**. In this chapter, the emulsion formulations, emulsification and processing conditions used are described. The equipment used to characterize the macroporous polymers produced are also explained in detail. Elements that belong or are related to a particular part of this work are included only in the relevant chapter.

The main purpose of the research presented in **Chapter 4** was to develop a method to produce macroporous beads and monoliths with controlled pore morphology. Emulsion templates were prepared using methyl methacrylate (MMA) and ethylene glycol dimethacrylate (EGDMA) in the continuous organic phase of the emulsion. Using MMA and EGDMA as monomer and crosslinker, macroporous beads with different internal pore structures were synthesized by controlling the internal phase volume ratio and surfactant concentration used to produce the emulsion templates. By controlling these parameters the transition zone from macroporous beads with closed pores to beads with an interconnected pore structure were identified. Also, in this chapter the stability over time and rheological behaviour of the emulsions formulated is described and analysed. Additionally, the mechanical properties of UV polymerized monoliths from the emulsion template are discussed. Finally, the thermal degradation behaviour in N₂ of the porous polymers produced is investigated and described. In **Chapter 5**, the surface and internal morphology of macroporous beads obtained through multiple emulsion templating was modified by changing the locus of initiation of the polymerisation and the initiator used. The objective of the work done in this part of the thesis was to create beads with a closed cell structure or surface as this will affect the encapsulation efficiency. The effect on bead surface structure of different electrolyte concentrations and the presence of a high HLB surfactant in the secondary aqueous phase used to create beads is also studied.

Chapter 6 describes a scalable method to produce large quantities of polymer beads with an improved production rate compared to microfluidics. This setup is based on a co-flow geometry, which we call “macrofluidic plug flow reactor”. The encapsulation capacity of the beads produced using this technique is tested by using an aqueous electrolyte or diluted HCl as model active ingredient in the dispersed phase of several emulsion templates. The morphology of the beads produced and the amount of encapsulated HCl is investigated. The macrofluidic device developed along with the suitable formulations engineered in Chapter IV are disclosed in a patent (EP16196601.5) filled at the end of 2016.

Chapter 7 discusses the efforts to improve the encapsulation rate of active ingredients in multiple emulsions by reducing diffusion, leading to beads with higher encapsulation efficiency after polymerization. The technique previously mentioned, allowed the production of macroporous beads by polymerisation of W/O emulsions without the need of a secondary aqueous phase. Again, HCl was used as model active ingredient to quantify the encapsulation potential of this technique. After 24 h of leaving the beads in open air at room temperature or in a sealed container, the amount of encapsulated HCl was quantified.

The results obtained in this thesis provide an alternative for the production of large volumes of macroporous beads with controlled size and size distribution. The overall conclusions derived from this thesis are presented in **Chapter 8** along with future work.

Chapter 2. Literature Background

2.1 Introduction

Polymer foams are commonly used in many aspects of modern life, to the point that is unlikely that a day passes without coming into contact with them. Polymer foams are used in various industries, such as automobile, aerospace, packaging and construction to name a few. This is due to their light-weight, excellent strength/weight ratio, low thermal conductivity and high dissipation of impact energy.²² The development of polymer foams started in the 1930's and -40's²³. The first patent for foamed polystyrene was filled in 1931 by the Swedish inventors Munters and Tandberg.²⁴ More recently, polyurethane foams occupy the largest market share in the US (53 %) in terms of amount consumed, while foamed polystyrene is second (26 %).²⁵ Depending on the specific requirements needed, other common polymers can be used to produce foams, such as epoxy resins, polyethylene, polypropylene, poly(acrylonitrile butadiene styrene), polyvinyl chloride (PVC) and silicone among others.²⁶ The characteristics of a foam are not only defined by the polymer used but also by its internal morphology, which can be composed of either close or open pores.²⁷ Polymeric foams are commonly produced by dispersing a gas within a polymer matrix, in a process called foaming. This process is based in the formation of gas by a blowing agent in a polymer matrix or at the same time as the material polymerises (gelation). However, the foaming process often requires the use of physical and chemical blowing agents, such as hydrofluorocarbons (HCFs) which were recently banned by an amendment to the Montreal Protocol,²⁸ volatile hydrocarbons and alcohols or super critical carbon dioxide.²⁶ Additionally, foaming does not provide good control of porosity and products often exhibit non-uniform pore structures.²⁹

An alternative technique for the production of polymer foams with controlled porosity, pore size and pore throat sizes is the use of emulsion templating. This technique is interesting for a wide range of applications, such as reaction supports³⁰ and chromatography columns.³¹ Basically, an emulsion containing monomers in the continuous phase is polymerised. After polymerisation, the internal template phase is removed, revealing a macroporous polymer with a pore morphology defined by the structure of the emulsion template at the gel-point of the polymerisation.³²

The aqueous template phase is usually removed by purification after polymerisation of the continuous phase of the emulsions. Therefore, considerable amounts of purifying solvent and energy are required to remove the templating phase from large volumes of polymeric materials with high porosities,* which can be a restricting condition for large production scales.³³ However, emulsion templating could be used to produce porous polymers encapsulating active ingredients which are part of the templating phase, the extraction of the dispersed in this case is not needed.³⁴ More recently, the application of macroporous materials produced from emulsion templates is being explored in fields, such as cell culture³⁵, tissue engineering³⁶ and carbon capture³⁷ to name but a few. Emulsion templating allows to control of the material morphology by varying the composition of the emulsion templates. This chapter introduces the fundamentals of emulsion templating for the synthesis of macroporous polymers. Additionally, the traditional and more recently developed methods used to produce macroporous polymer beads from emulsion templates are reviewed. Also, the literature concerning encapsulation of active ingredients in multiple emulsions and later in macroporous beads is discussed.

2.2 Formation and classification of emulsions

An emulsion is a dispersion of one immiscible liquid, as droplets, in a second liquid (e.g. water and oil), created by dispersing one phase in the other. The droplet break-up mechanism used to emulsify the emulsion components can be either stirring, shaking, blending, ultrasonication, or membrane emulsification.³⁸ Additionally, if the interfacial tension between the phases is sufficiently low spontaneous emulsification can also occur, such is the case for microemulsions.³⁹ Emulsions can be classified as oil-in-water (O/W) or water-in-oil (W/O) emulsion; the first mentioned phase denotes the dispersed phase. It is also possible to form non-aqueous emulsions by dispersing a polar liquid into an immiscible nonpolar liquid, and vice versa i.e replacing the aqueous phase for eutectic solvents⁴⁰ or ionic liquids.⁴¹ These emulsions are referred to as oil-in-oil (O/O) emulsions.⁴² Emulsions are important in a broad range of industries, such as oil extraction and petrochemistry, food, agriculture, textile and pharmaceutical just to name a few.⁴³⁻⁴⁴ The preparation and properties of emulsions have

* The amount of energy required to remove the water from a macroporous polymer with a porosity of 80 % and a foam density of 200 kg/m³ was estimated in 929 kJ/kg of polymer.

been widely investigated, the ability to understand these properties is essential in the design and operation of equipment related to those applications i.e design, operation, manipulation, storage, etc. Emulsions can be classified according to the amount of internal phase volume ratio (ϕ). Emulsions with less than 34 % internal phase volume ratio are called low internal phase emulsions (LIPes), while emulsions between 34 and 70 % internal phase volume ratio are called medium internal phase emulsions (MIPEs).⁴⁵⁻⁴⁶ Above an internal phase volume ratio of 70 %, emulsion are denominated high internal phase emulsions (HIPEs). However, in recent times, emulsions containing an internal phase volume ratio that exceeds 74.05 % are defined as HIPEs, since this value represents the maximum packing of monodisperse rigid spheres.^{32, 47} This kind of emulsions are usually highly viscous.⁴⁷ This is explained by the close-packed configuration along with the interaction between adjacent droplets. These effects cause a resistance of the emulsion to flow due to the difficulty for droplets to easily slip past each other. In emulsions with an internal phase volume ratio above 74.05 % the droplets are, either deformed into a rhomboidal dodecahedron⁴⁵ (Figure 2-1) or polydisperse in size.⁴⁸

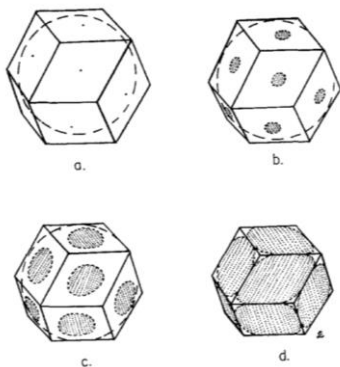


Figure 2-1. Deformation from spherical droplet to rhomboidal dodecahedron⁴⁵

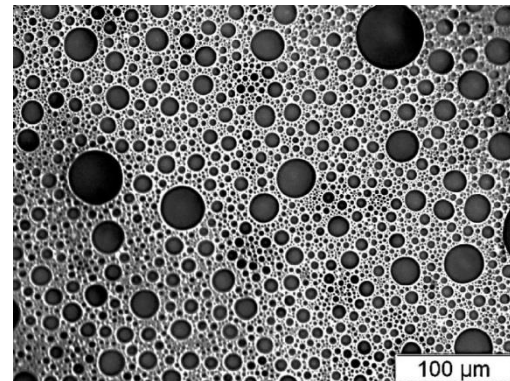


Figure 2-2. HIPE with an internal phase volume ratio of 75 %⁴⁹

Above an internal phase volume ratio of 96.4 %, monodisperse emulsions will experience a change in the internal geometry adopting a tetrakaidecahedral packing. The typical outcome in the production of HIPEs using conventional intensive mixing devices is the formation of emulsions with a broad size distribution or polydispersity (Figure 2-2) as a result of the non-uniform shear applied during emulsification. However, theoretical calculations showed that after an adequate energy input during emulsification HIPEs tend to monodispersity.⁴⁸ This is due to the fact that, in polydisperse emulsions as ϕ increases (especially for $\phi > 0.88$), smaller

droplets must be distorted to a greater degree than larger droplets, because larger droplets are more difficult to deform. The highly distorted small droplets tend to coalesce due to a higher Laplace pressure than larger droplets, supporting the tendency towards monodispersity.⁵⁰ Monodisperse emulsions can be produced using various methods, such as fractionation⁵¹, controlled shear rupturing⁵² and more recently microfluidic emulsification reaching a droplet size coefficient of variation low as <3 %.⁵³

2.2.1 Stabilisation of emulsions and use of emulsifiers

Emulsions are by nature thermodynamically unstable. They tend to minimise the free energy which drives minimisation of the interfacial area; this procedure promotes phase separation. Depending on the requirements of the application, emulsions can be considered stable if they can resist physical changes over a practical length of time that can vary from a few days, months or even years.⁵⁴

Emulsifiers, such as surfactants or particles have been widely used to extend the life time of emulsions. They are used to stabilise emulsions by adsorbing at the liquid/liquid interface, generally but not necessarily lowering the interfacial tension. The use of emulsifiers provides enhanced stability to emulsion systems by creating an electrostatic or steric barrier which prevents close approach of the droplets, protecting against agglomeration and coalescence. Surface active agents or surfactants consist of amphiphilic molecules that possess a hydrophilic and a hydrophobic component (Figure 2-3). This compounds lower the interfacial tension and hence the amount of energy required for emulsification.

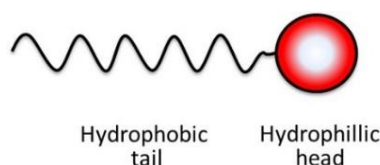


Figure 2-3. General structure of a W/O surfactant molecule

They form a steric (mechanical) barrier around the droplets stabilising the emulsion against agglomeration and coalescence (Figure 2-4). The affinity of surfactants to promote the formation and stabilisation of W/O or O/W emulsion is generally defined by the hydrophilic-hydrophobic balance (HLB).⁵⁵ The HLB value of a surfactant, a scale developed by Griffin spanning from 1 to 40,⁵⁶ is based on the relative percentage of hydrophilic to lipophilic

(hydrophobic) groups in a surfactant molecule. The semiempirical HLB method is widely used for classifying surfactants and aiding with the surfactant selection. However, the HLB value does not allow the prediction of the efficiency or the effectiveness of a surfactant to stabilise an emulsion.

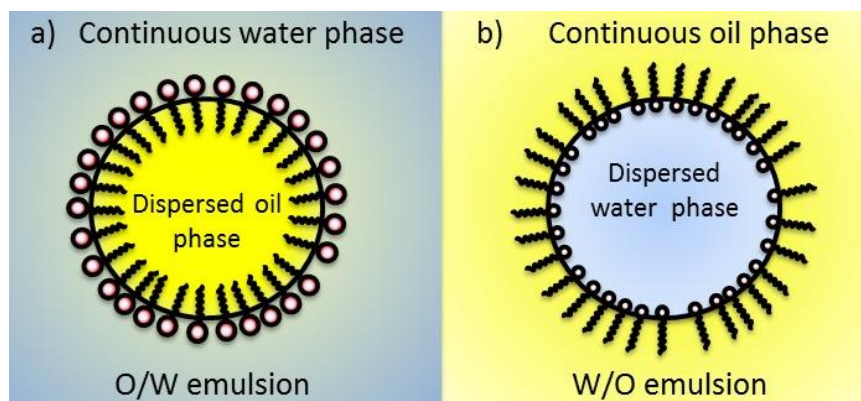


Figure 2-4. Schematic representation of surfactant stabilised droplets a) Droplet of an O/W emulsion stabilised by surfactant with a high HLB (typically between 8 and 18); b) Droplet of a W/O emulsion stabilised using surfactant with a low HLB (typically between 2 and 6).

Surfactants with a HLB value between 2-6 (in one of the first patents for macroporous polymers from emulsion templates filled by Unilever a value of 4 was preferable for long term stability)⁵⁷ could promote the formation of W/O emulsions.⁵⁸ In case of O/W emulsions the surfactant should have intermediate to high HLB values ideally between 8 and 18. In the case of M/HIPEs, which will be mostly discussed in this thesis, are usually stabilised using large amounts of surfactant (4-50 vol.%).⁵⁹ However, more recently novel surfactants developed by Mork et al.⁶⁰ and patented by Dow have proven effective for the stabilisation of HIPEs with concentrations below 1 vol.%.

Particle stabilised or Pickering emulsions

An alternative to stabilise emulsions is the use of colloidal particles. These emulsions were first described by Ramsden in 1903.⁶¹ Later, particle stabilised emulsions were systematically studied by Pickering,⁶² therefore they are often named Pickering emulsions. Emulsion can be stabilised using different inorganic particles, such as modified silica,⁶³⁻⁶⁵ titanium oxide nanoparticles,⁶⁶⁻⁶⁷ magnetic nanoparticles,⁶⁸⁻⁶⁹ carbon nanotubes (CNT)⁷⁰ or graphene oxide.⁷¹ Also, organic colloidal particles, such as protein fibrils,⁷²⁻⁷³ polymeric particles,⁷⁴⁻⁷⁶ and more recently particles derived from cellulose, such as cellulose nanocrystals,⁷⁷ bacterial cellulose

fibres⁷⁸ or starch nanoparticles,⁷⁹ can be used to emulsify stable emulsions. Colloidal particles are used to stabilise emulsions by adsorbing at the liquid interface between the dispersed and continuous phase of the emulsion. Unlike surfactants, particles do not affect the interfacial tension but stabilise the emulsion by forming a solid barrier at the interface. Therefore, the most important parameter for emulsion stability is the wettability of the particles. Hydrophilic particles with contact angles θ_{ow} of less than 90° (Figure 2-5a) have a larger fraction of the particle in the aqueous phase, and therefore, tend to form O/W emulsions. In the same way as surfactants, the larger area of the particle surface will remain on the external side curving the particle monolayer. On the other hand, hydrophobic particles promote the formation of W/O emulsions as θ_{ow} is greater than 90° (Figure 2-5c).⁸⁰

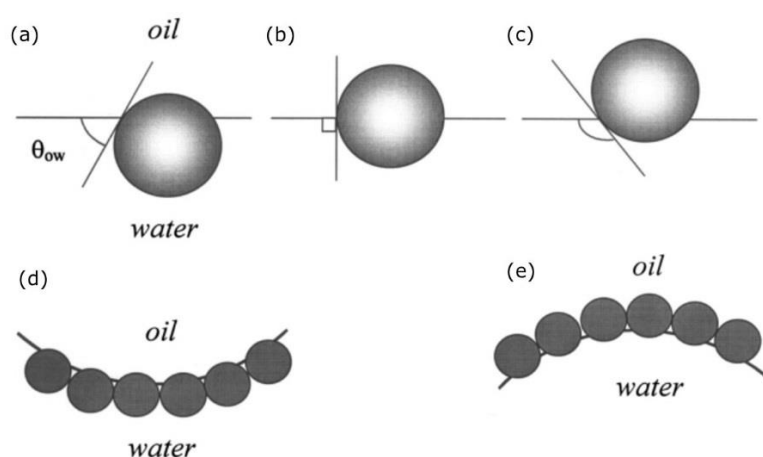


Figure 2-5. Schematic of particles with different contact angles at an oil-water interface (a) Hydrophilic spherical particle, the contact angle is $90^\circ > \theta > 0$. (b) Particle with a contact angle of 90° (c) Particle with a contact angle $180^\circ > \theta > 90^\circ$. (d) Possible positioning of hydrophilic particles at a curved interface. (e) Possible positioning for hydrophobic particles at an interface.⁸⁰

The emulsion stability is achieved when the contact angle between solid particle, water and oil phases is approximately 90° (but not equal). This is caused by the strong particle attachment to the liquid interface.⁸¹⁻⁸² When the particles are either too hydrophilic or too hydrophobic they tend to remain dispersed in the bulk oil or aqueous phase instead of adsorb at the interface, leading to unstable emulsions. Often in particle stabilised or Pickering emulsions, the droplets are completely covered by particles reducing the free O/W interface area with a corresponding interfacial tension γ_{ow} and leading to a reduction of the energy of the complete system. Therefore when two droplets contact each other the particle layers formed prevent the coalescence of the droplets. This effect is denominated bilayer

stabilisation (Figure 2-6a). Coalescence can also be prevented by a monolayer of particles bridging the surfaces of neighbouring emulsion droplets (Figure 2-6b).⁸³⁻⁸⁴ Bridging stabilisation can explain the existence of very stable emulsions even when the droplets are sparsely covered with particles.⁸⁵⁻⁸⁶ Other possible particle configurations to stabilise emulsions droplets are the formation of aggregates; they can form a network on the droplet surface as presented in Figure 2-6c or isolated as shown in Figure 2-6d. Also it is possible that a 3D viscoelastic particle network is formed between emulsion droplets when a large amount of particles is used (Figure 2-6e), in this case also bilayer stabilisation is present but the particle network improves stability by preventing droplet contact and raising the viscosity of the continuous phase.^{81, 87}

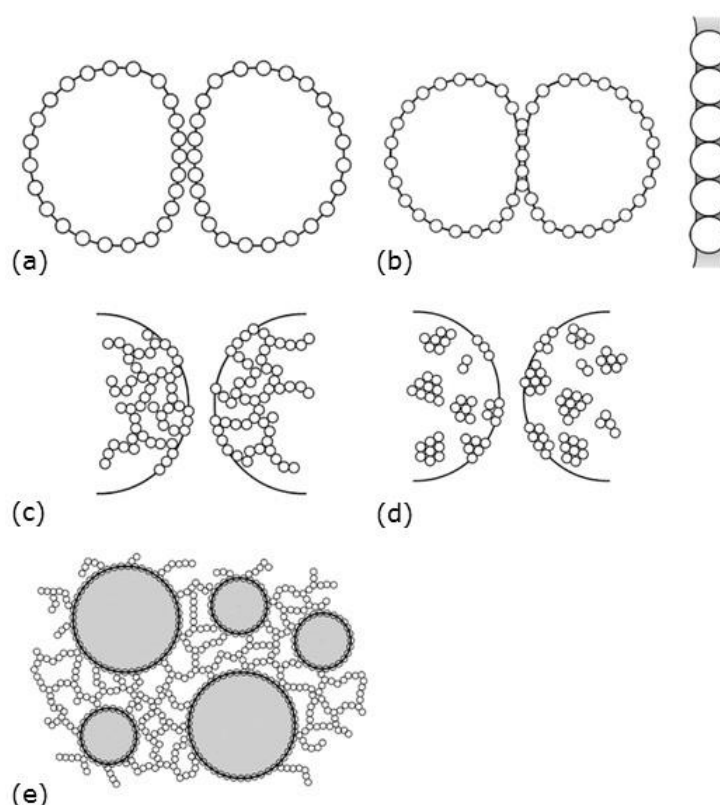


Figure 2-6. Representation of different stabilisation mechanism through particle configuration in Pickering emulsions.⁸³

Due to thermodynamic balance, when a particle migrates to the interface, the energy released after the particle is adsorbed is also the Gibbs free energy needed to remove the particle from the interface. If the particles are small enough then the effect of gravity can be ignored, the Gibbs free energy $-\Delta_{int}G$ (adsorption energy) needed to remove a particle of radius r from an into oil-water interface of tension γ_{ow} can be calculated using the following expression:⁸⁸

$$-\Delta_{int}G = \pi r^2 \gamma_{ow} (1 \pm \cos \theta_{ow})^2 \quad \text{Equation 2-1}$$

The sign inside the bracket is negative for removal of a particle into the water phase and positive for removal into the air or oil phase. For hydrophilic particles (contact angles less than 90°) the energy needed to remove the particles will be higher from the oil phase than from the water phase. If the particles have contact angles of more than 90° (hydrophobic particles), the opposite is true and it will be easier to remove the particles into oil than water. Based on this it can be said that the best adsorption of the particle at the interface will be achieved when the two liquid phases have a similar attraction towards the particles. For particles with a contact angle close to 90°, the adsorption energy is in the order of a few 1000 kT (the Boltzmann constant, k times the temperature T). This means that the energy needed to remove a particle from the interface is usually much greater than the thermal energy at room temperature and the particle can be considered irreversibly adsorbed at the fluid interface.⁸⁰ This explains the much lower temperature sensitivity, typical for particle stabilised emulsions when compared with surfactant stabilised emulsions. In the case of surfactant molecules, since $-\Delta_{int}G$ depends on the particle size, for particles of a similar size to most surfactants (<1 nm radius) the particle removal from the interface is easy (several kT) and, therefore, they may not be too effective as stabilisers.⁸⁹ Additional benefits of using particles as emulsifiers is that usually low particle concentrations (e.g. less than 1 wt.%) are required for producing stable emulsions.⁹⁰⁻⁹¹ Moreover, emulsions stabilised with particles, such as hydrophobic silica, can be inverted from W/O to O/W emulsions by increasing the volume fraction of water,⁹²⁻⁹³ unlike emulsions stabilised by a single surfactant.

Mechanisms of emulsion instability

The presence of emulsifiers at the emulsion interface delays emulsion phase separation. However, due to their essential unstable nature, emulsions may follow various destabilisation paths, leading to phase separation of the immiscible components. The mechanisms of emulsion destabilisation are shown in Figure 2-7. A normal dispersed emulsion is represented in Figure 2-7a. A common destabilisation process is caused by the aggregation of droplets that keep their original size (Figure 2-7b). This effect is called flocculation and is mainly driven by van der Waals attractions.⁹⁴ Creaming and sedimentation (Figure 2-7c) are caused by the density differences of the two liquids when the dispersed droplets experience a vertical force

due to the gravitational field. If the dispersed droplets precipitate due to a higher density than the continuous phase the term sedimentation is used. However, if due to lower density the droplets ascend, the term creaming is used. Both effects lead to a concentration gradient along the vertical direction in the emulsions. This effect is reduced in emulsions with a high volume ratio due to interaction among droplets and thus caused less droplet motion in the emulsions.⁹⁵ Another destabilisation mechanism denominated Ostwald ripening (or disproportionation) is the constant diffusion of the dispersed phase through the continuous phase from small to large droplets (Figure 2-7d). This effect increases the average droplet diameter while reducing the amount of droplets stimulating the formation of two macroscopic immiscible phases that finally end in phase separation (Figure 2-7f). This constant diffusion of matter takes place due to differences in the chemical potential of molecules within droplets of different sizes (the chemical potential of molecules within a droplet is inversely proportional to the droplet size). Ostwald ripening can be reduced by using electrolytes, such as sodium chloride,⁹⁶ potassium sulphate,⁹⁷⁻⁹⁸ magnesium sulphate,⁹⁹⁻¹⁰⁰ and calcium chloride in the aqueous phase of the emulsion.¹⁰¹ This effect can also be promoted by the addition of porogens in the internal aqueous phase leading to emulsions with a larger droplet size.

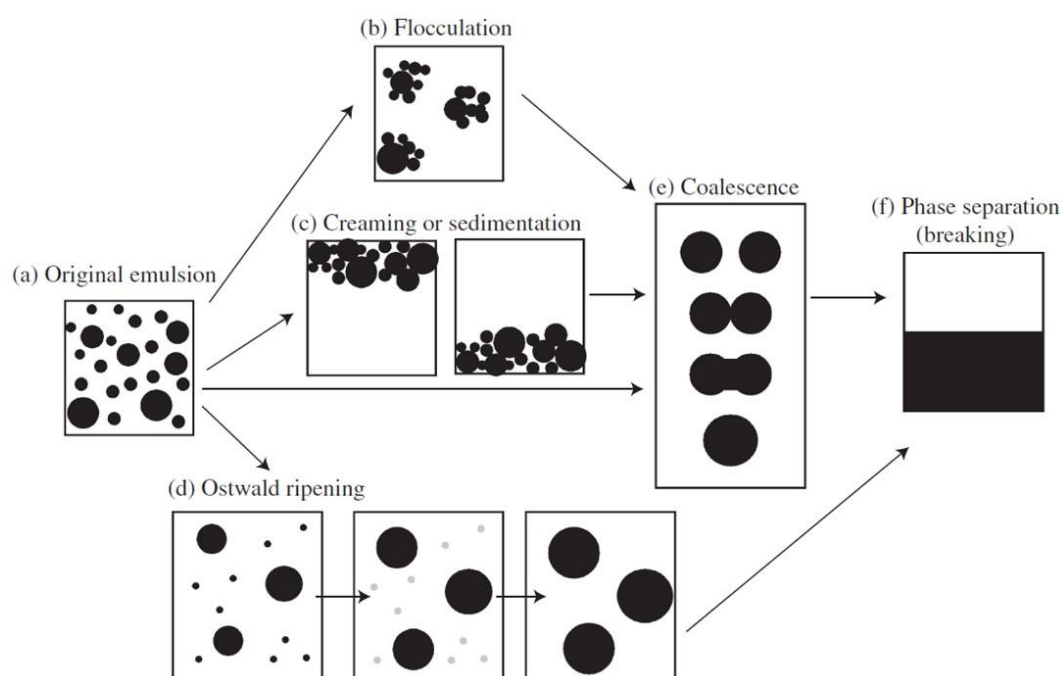


Figure 2-7. Schematic representation of different destabilisation mechanism of emulsions.⁸³

The coalescence of the droplets (Figure 2-7e) is process in which the thin liquid film between two neighbouring droplets ruptures. This break in the continuous phase will grow until the two droplets of internal phase fuse and results in phase separation (Figure 2-7f).⁹⁴ In emulsions various destabilisation mechanisms can occur simultaneously making the analysis of the causes more complicated.

2.3 Multiple emulsions

Double or multiple emulsions are emulsions that contain in their dispersed phase droplets of a different phase. It is possible to produce at least two types of double emulsions, namely water-in-oil-in-water ($W_1/O/W_2$) emulsions and oil-in-water-in-oil ($O_1/W/O_2$). A $W_1/O/W_2$ multiple emulsion consists of small droplets of an internal aqueous solution (W_1) dispersed within an organic phase (O) which is dispersed in a secondary or external continuous aqueous phase (Figure 2-8).

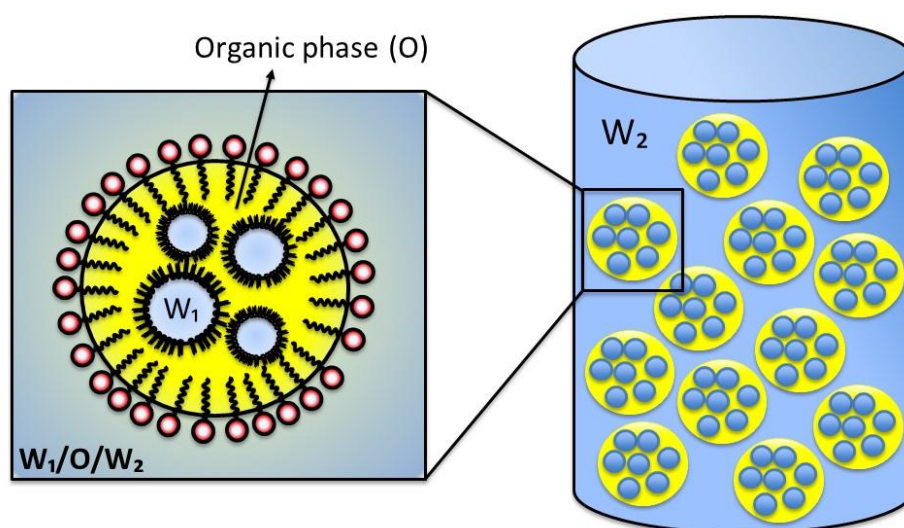


Figure 2-8. Schematic of a $W_1/O/W_2$ multiple emulsion. Hydrophilic and lipophilic surfactants are used to stabilise the interfaces.

The capacity of surfactants to reduce the interfacial tensions is a vital property that makes them suitable for the stabilisation of multiple emulsions. The hydrophilic-lipophilic balance (HLB) of a surfactant molecules determines the ability of the surfactant to stabilise a specific interface (W/O or O/W) of the emulsions to be formed.⁵⁵ Usually, W_1/O emulsions are stabilised using surfactants with a HLB between 2 and 6. The W_1/O emulsion is then dispersed

into a secondary aqueous solution typically containing surfactants with HLB between 8 and 18 to form a $W_1/O/W_2$ emulsion.⁹⁴ Multiple emulsions were first reported by Seifriz¹⁰² in 1925 and both $O/W/O$ and $W/O/W$ types have many potential applications in a wide range of fields, such as oil extraction and petrochemistry, cosmetics, pharmaceutical, agriculture and food industry to name a few, mainly with the purpose of encapsulation and protection systems for controlled release of active compounds.^{54, 103} Furthermore, multiple $O_1/O_2/O_1$ and $O_1/O_2/W_1$ emulsions have been prepared by dispersing polar oil droplets into a nonpolar oil, which can be dispersed into a secondary phase consisting of another polar oil¹⁰⁴ or an aqueous solution.¹⁰⁵

2.3.1 Stabilisation of multiple emulsions

Multiple emulsions are inherently thermodynamically unstable systems, even more than regular emulsions, and their stabilisation can be quite difficult.¹⁰⁶ Controlling the surfactant migration and osmotic balance between the dispersed internal droplets and the external continuous phase are key to achieve an optimal stabilisation. Therefore, the selection of a suitable surfactant is essential.¹⁰⁷ The influence of the surfactant systems on the stability of multiple emulsions is defined not only by the surfactants concentration but also by the structure of the surfactants, which determines HLB.¹⁰⁷⁻¹⁰⁸ More recently W_1/O HIPEs were used to create $W_1/O/W_2$ multiple emulsions after phase inversion by Li et al.¹⁰⁹, the multiple emulsions synthesised in this case were stabilised using only one surfactant (12-acryloxy-9-octadecenoic acid). After polymerisation of the organic phase of the multiple emulsions, which contained styrene or acrylates as organic phase, polyHIPE beads with diameters in the order of 20 μm were produced. Besides using surfactants, multiple emulsions can be stabilised by colloidal particles with the right hydrophobicity, such as SiO_2 , clay or zinc oxide among others.¹¹⁰ As for simple emulsions, besides the emulsifier used, the stability and rheological properties of multiple emulsions are influenced by the internal phase volume ratio¹¹¹ and droplet size.¹¹²

The more frequent destabilisation processes in $W_1/O/W_2$ multiple emulsions can be described as follows:

- Diffusion of electrolytes or active ingredients dissolved in the internal droplets (W_1) to the external continuous phase.
- Coalescence of W_1 droplets resulting in the formation of a W/O emulsion.

- Expulsion of W_1 droplets to the external aqueous phase leading to phase inversion of the emulsion resulting in an O/W emulsion.

- Flocculation of the W_1 and W_1/O droplets leading to modification of the multiple emulsion rheological properties i.e., an increase in the viscosity of the entire system.

Practical applications of $W_1/O/W_2$ multiple emulsions have been limited by their thermodynamic instability. Attempts to improve their stability have been made by exploring various approaches, such as using polymeric surfactants to create an enhanced interface coverage and a better anchor into the dispersed phases^{113, 114} and controlling the droplet size by emulsification, for instance using microfluidic systems.¹¹⁵

2.4 Rheology of emulsions

It is important to understand the rheological properties of emulsions as they can provide information about critical parameters, such as stability and emulsion structure.¹¹² There are several factors that affect the rheological behaviour of emulsions, such as colloidal interactions, internal phase volume ratio, the emulsion composition, interfacial properties, droplet size and size dispersion to name a few.³⁹ The viscoelastic properties of emulsions are investigated by applying a sinusoidal stress at a frequency ω to the system and measuring the response (Figure 2-9a). In the linear regime, where stress and strain are proportional, the response of the emulsion is also sinusoidal and the strain rate lags behind the applied stress by a phase angle δ .

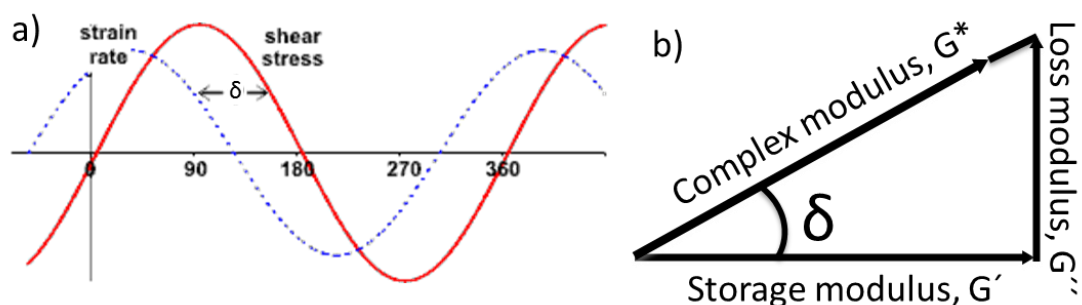


Figure 2-9. a) Schematic of a typical stress and strain wave relationships for a viscoelastic material. Solid line is the shear stress and dotted line the strain rate. b) Relationship between viscous (loss modulus G'') and elastic (storage modulus G') contributions to the complex modulus G^* .¹¹⁶

The response of the system can be conveniently represented in terms of a complex number, the shear modulus $G^*(\omega)$, which is a quantitative measure of material stiffness or resistance

to deformation (Figure 2-9b). The shear modulus $G^*(\omega)$ is the ratio of the shear stress to the shear strain and can be written as Equation 2-2:

$$G^*(\omega) = G' + jG'' \quad \text{Equation 2-2}$$

where G' is the storage modulus, G'' represents the loss modulus and j is the imaginary number $\sqrt{-1}$. The $\tan(\delta)$ parameter is an important indicator of rheological behaviour of the emulsions and is used to quantify the balance between energy loss and storage (Equation 2-3).

$$\tan(\delta) = G''/G' \quad \text{Equation 2-3}$$

In materials with a pure elastic behaviour (all energy stored in the material), as δ approaches zero, the storage modulus (G') will tend to 1 and the loss modulus (G'') will tend to 0. As δ approaches 90° , that is maximum phase shift and pure viscous response (all energy dissipated as heat), then $G'=0$ and $G''=1$. Viscoelastic materials having both characteristics will have a δ value between 0 and 90° , with 45° representing the boundary between solid-like and liquid-like behaviour.

Due to the variety of emulsions with different internal phase volume ratios (ϕ) used in this work, a basic explanation on emulsion rheology and the changes in rheological behaviour with increasing ϕ is presented.

Rheological behaviour of dilute emulsions

Dilute emulsions are systems where the internal phase volume ratio ϕ is less than 0.02.¹¹² In this kind of emulsion, the droplet behaviour can be modelled as if they were in an infinite continuous phase with no interaction between neighbouring droplets. Several reviews that include the models describing the rheological behaviour of such systems can be found in the literature.^{55, 112, 117} For more concentrated emulsions, the equations describing the rheological behaviour of dilute systems cannot be applied as the interaction between the neighbouring droplets plays an important role.

Rheological behaviour of M/HIPEs

Medium internal phase emulsions (MIPEs) or moderately concentrated systems have a concentration of internal phase that allows the interaction between droplets without forming a closely packed system (ϕ less than 0.64). The interactions between droplets of internal phase can be attractive (primarily due to van der Waals or hydrophobic forces) or repulsive with mainly steric or electrostatic forces involved. The maximum concentration of internal phase for this region (ϕ^*), assuming monodisperse and non-deformable droplets varies with the packing geometry of the droplets. For an internal phase volume ratio between $0.58 < \phi < 0.64$ (Figure 2-10) the free movement of the droplets becomes severely restricted as they are trapped or “caged” between neighbouring droplets and only separated by a thin layer of continuous phase.¹¹⁸

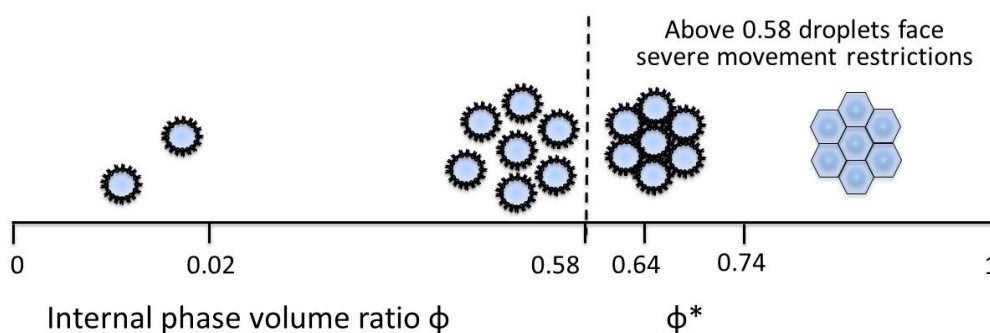


Figure 2-10. Schematic representing the arrangement transitions in monodisperse emulsions with increasing internal phase volume. Adapted from Mason et al.¹¹⁹

In these systems the droplet can only vibrate or oscillate between neighbouring droplets so there is no smooth flow of droplets passing each other. When ϕ exceeds 0.64 a dramatic increase in viscosity and viscoelastic behaviour is observed. The maximum internal phase volume ratio (ϕ^*) for non-deformable monodisperse droplets theoretically, is either ≈ 0.64 for a randomly close packing or approximately ≈ 0.74 for a hexagonal close packing of uniform spheres. Above an internal phase volume ratio of 0.74, the monodisperse droplets will deform from a spherical shape into a close packed structure with polygon – shaped droplets.⁴⁸ The work used to create this deformation in the droplets is equivalent to the elastic energy stored due to an increase in the total surface area of the interface.¹²⁰ But on the other hand, deformation of the droplet surface causes a reduction in droplet curvature and therefore in the capillary pressure. This effect will be addressed later in this chapter.

Only semi - empirical equations are available for describing the rheology of emulsions of intermediate volume fractions (without droplet deformation).¹²¹⁻¹²² An early model was developed by Oldroyd,¹²³⁻¹²⁴ which was valid at small variable strain rates for emulsions of two immiscible Newtonian liquids with constant interfacial tension. This equation (Equations A2-1 to A2-4 in Annex I-support information) predict emulsions to be viscoelastic in oscillatory shear flow. In steady shear flow, the Oldroyd model predicts a shear-thinning behaviour. However, the Oldroyd model is valid for moderately concentrated emulsions where $\phi < 0.2$. A more recent empirical model that describes the viscoelastic properties (storage and loss modulus) over a broad range of internal phase volume ($0 \leq \phi \leq 0.64$) was developed by Pal.¹²⁵ In this model (Equation 2-4) the actual volume fraction ϕ is replaced by an effective volume fraction in order to consider the “crowding” effect of droplets¹²⁶ (caused by packing difficulties of particles i.e. homogeneous distribution of the droplets, such as clustering or aggregation or other interactions among adjacent droplets) and the packing limit. From this measurement the complex modulus $G^*(\omega)$, the storage modulus G' (the elastic component) and the loss modulus G'' (the viscous component) can be obtained:

$$G^*(\omega) = G_m^*(\omega) \left[\frac{1+3\psi\phi H^*(\omega)}{1-2\psi\phi H^*(\omega)} \right] \quad \text{Equation 2-4}$$

where $G^*(\omega)$ is the complex shear modulus of an emulsion of uniform droplet size when subjected to an oscillatory strain of small amplitude, $G_m^*(\omega)$ the complex shear modulus of the matrix or continuous phase of the emulsion and $\psi\phi$ the effective volume fraction. The equations to calculate the effective volume fraction and the term H^* are included in the support information as Equation A2-5 and Equation A2-6. For emulsions with an internal phase volume ratio between 0.6 and 0.8, an analytical model was recently developed by Mason and Sheffold¹²⁷ to calculate the elastic shear modulus effect in emulsions with in droplet sizes between 5 μm and 5 nm. The elastic behaviour observed is due to elasticity of shape of the interface governed by interfacial tension.

Rheological behaviour of High Internal Phase Emulsions (HIPEs)

In HIPEs the internal phase volume ratio ϕ exceeds the maximum packing volume ratio of monodisperse spheres. As ϕ increases and reaches the maximum packing volume ratio non-deformable spherical droplets, significant changes in the rheological properties of the

emulsion can be observed, namely a transition from Newtonian viscous flow of diluted emulsions to a viscoelastic behaviour. Typically HIPEs have a higher viscosity relative to the bulk liquid phase of its components but a decrease in viscosity can be observed when a narrow range of stress is applied. This abrupt transition in the viscosity reflects the rupture of the emulsion structure, indicating a stress limit known as yield stress. The yield stress (τ_0) is the shear stress needed to induce flow; below that limit emulsions behave as viscoelastic solids. On the other hand, above the yield stress HIPEs behave as shear-thinning liquids in which the viscosity drops with increasing shear rate.³² An example of the changes in the rheological behaviour of emulsions in the transition zone above randomly close packing and hexagonal close packing of non-deformable spherical drops ($\phi = 0.64$ and $\phi = 0.74$ respectively) is observed in Figure 2-11, which represents the variation of apparent viscosity with shear stress for emulsions at different volume fractions.

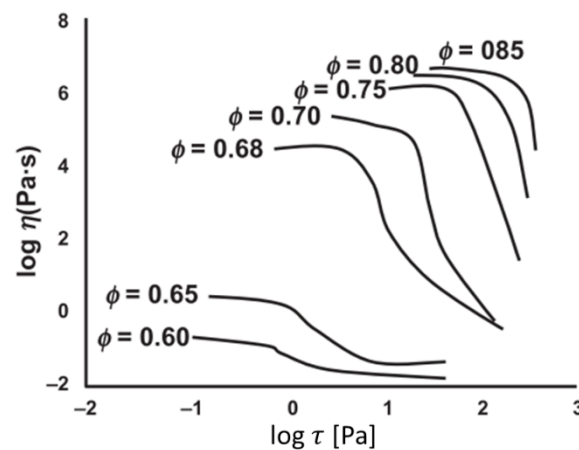


Figure 2-11. Example of flow curves for W/O emulsions in a wide range of internal phase volume ratios. The figure shows the dramatic change in rheological properties of emulsions when the internal phase volume ratios approaches the concentration limit for close packing of monodisperse spherical droplets.

117, 128

The stress/strain behaviour related to the internal phase volume fraction (ϕ), the interfacial tension (γ), contact angle (θ) associated with the thin films separating adjacent droplets,¹²⁹ the thickness of the films separating adjacent droplets and droplets radius (R) in the elastic region was investigated by Princen.¹³⁰ By modelling emulsions composed of same sized drops (Equations A2-7 and A2-8 in the supporting information), it was found that yield stress (τ_0) and static shear modulus (G) are directly proportional to the interfacial tension and inversely proportional to the droplet radius. Moreover the yield stress (τ_0) and static shear modulus

both increases with increasing internal phase volume fraction ϕ and increases in interfacial tension. These effects originate in the increased deformation of the droplets that leads to a higher resistance to flow, as the droplet movement is restricted. The empirical equations 2-5 and 2-6 were proposed by Princen and Kiss^{129, 131} to model the yield stress and static shear modulus in highly concentrated emulsions:

$$\tau_0/(\gamma/R) = \phi^{1/3}[-0.08 - 0.114 \log_{10}(1 - \phi)] \quad \text{Equation 2-5}$$

$$G/(\gamma/R) = 1.769\phi^{1/3}(\phi - 0.712) \quad \text{Equation 2-6}$$

where γ is the interfacial tension and R is the Sauter mean radius of emulsion droplets, defined as:

$$R = \frac{\sum n_i R_i^3}{\sum n_i R_i^2} \quad \text{Equation 2-7}$$

where n_i is the number of droplets of radius R_i .

As ϕ increases, the internal phase droplets deform more and more into a polyhedral shape creating a crowding effect. Due to this effect, when a small rate of shear deformation is applied to the emulsion, it behaves as a purely elastic solid (represented by the storage modulus, G') until the yield stress is reached and the system adopts a shear thinning behaviour. However, the relations developed by Princen and Kiss do not consider the thickness of the layer separating individual droplets. Therefore, equations 2-5 and 2-6 are valid only for emulsions where the influence of the liquid film between neighbouring droplets can be ignored. The effect of a finite film thickness can be considered by using the effective internal phase volume ratio (ϕ_{eff}) instead of ϕ .¹³⁰ The relationship between (ϕ_{eff}) and ϕ presented by Princen¹²⁹ is as follows,

$$\phi_{\text{eff}}^{-1/3} = \phi^{-1/3} - 1.105 \frac{h}{D} \quad \text{Equation 2-8}$$

where h is the film thickness and D the average droplet diameter.

General rheological behaviour of emulsions with increasing internal phase volume ratio ϕ

A general representation of the variation of the rheological properties of emulsions with increasing internal phase volume ratio (from dilute to highly concentrated emulsions) was presented by Derkach¹¹⁷ and it is shown in Figure 2-12. In this figure, the region I represents dilute emulsions exhibiting a Newtonian behaviour with constant viscosity; in region II the emulsions show a weak non-Newtonian behaviour due to droplet interaction; in region III strong non-Newtonian effects can be expected with thixotropic and viscoelastic effects; region IV represents the behaviour of emulsions with $\phi > \phi^*$, this is where HIPEs are located. HIPEs behave as viscoplastic liquids with a yield stress and wide frequency range of elasticity with constant shear modulus. Typical concentration dependencies of the elastic modulus G , and yield stress τ_0 are shown, this kind of linear dependence of ϕ is consistent with the proposals of Princen and Kiss.¹²⁹

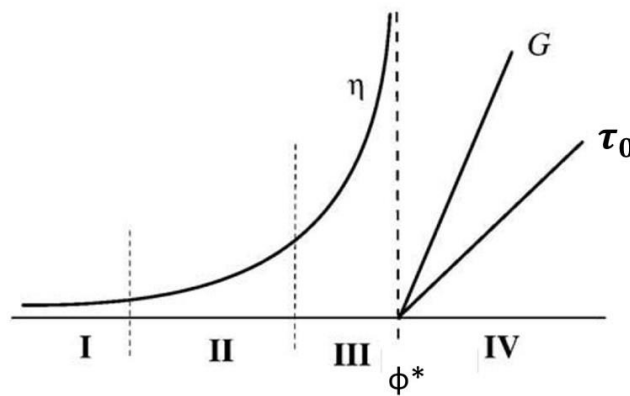


Figure 2-12. Schematic of typical rheological behaviour of emulsions across the entire internal phase volume ratio. The viscosity (η) is constant for dilute emulsion (region I), as the internal phase volume ratio increases (region II and III) non-Newtonian behaviour is observed. Above the critical internal phase concentration ϕ^* (region IV) highly concentrated emulsions are formed and the materials exhibit a relation between elastic modulus (G), yield stress (τ_0) and internal phase concentration (ϕ).¹¹⁷

Further rheological measurements have indicated that HIPEs show both nonlinear viscoelastic and viscous behaviour (Figure 2-13).¹³² For a defined internal phase volume ratio, the complex modulus G^* remains almost constant. As the stress increases, a critical boundary is reached which indicates the limits of the linear viscoelastic domain where the stress is not sufficient to disrupt the structure of the emulsions. A further shear increase results in a rapid decrease of G^* , indicating the onset of the nonlinear domain for which changes in structure begin to occur. The rapid decrease of G^* indicates a “softening” or relaxation of the microstructure of the

emulsion. This behaviour is also observed in colloidal dispersions that undergo destruction of the structure when the stress exceeds a critical value.^{117, 128}

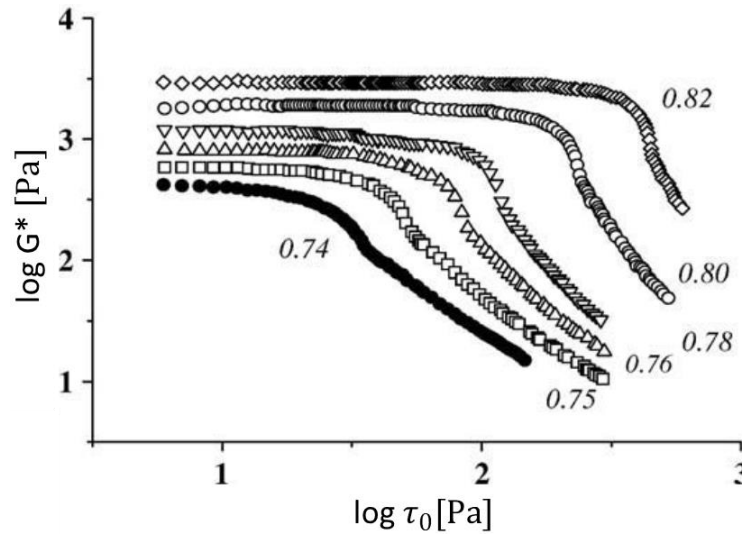


Figure 2-13. Typical flow curves of highly concentrated emulsions showing the shear stress (τ) dependence of shear modulus G^* for emulsions with increasing internal phase volume ratios. Adapted from ^{117, 132}

The analysis of the viscous behaviour of high internal phase emulsions is more complex compared with the elastic and yield behaviours. A two-dimensional theoretical model describing the viscosity of concentrated emulsions and foams was presented by Schwartz and Princen.¹³³ This two dimensional model was later extended for three dimensional systems in steady shear flow^{131, 134} and Equation 2-9 was proposed to calculate the steady shear viscosity:

$$\eta = \frac{\tau_0}{\dot{\gamma}} + 32(\phi - 0.73)\eta_c(N_{Ca})^{-1/2} \quad \text{Equation 2-9}$$

where η_c is the viscosity of the matrix or continuous phase, N_{Ca} the capillary number, $\dot{\gamma}$ the critical shear rate where bridging flocculation occurs and τ_0 the yield stress. Equation 2-8 is only valid for $N_{Ca} < 10^{-4}$.

2.5 Emulsion templating as route to create macroporous materials

Polymerisable emulsions can be used to create highly porous materials, such as porous polymers,¹³⁵ carbons¹³⁶, ceramics¹³⁷ and other inorganic materials¹³⁸ with tailored characteristics through a technique named emulsion templating. In order to produce porous

polymers, the continuous phase of the emulsion is polymerised, therefore the solid material produced will adopt the morphology of the emulsion.⁵⁷ After solidification of the continuous phase the internal templating phase of the emulsion is removed revealing a material with a porous structure. The morphology of the material is defined by the structure of the emulsion template at the gel-point of the polymerisation.³² The use of M/HIPES as templates to produce porous materials was described by Bartl and von Bonin¹³⁹ at the beginning of the 1960s. Later, these materials were denominated PolyM/HIPES, a term coined by Unilever scientists in one of the first patents claiming the production of low density polymeric materials through emulsion templating, filled in the early 1980s.⁵⁷ PolyM/HIPES are characterised for being light, with porosities up to 99 % and apparent densities as low as 12.6 kg/m³.¹⁴⁰ PolyHIPES have been explored for different applications, such as scaffolds for tissue engineering,¹⁴¹⁻¹⁴² cell culture¹⁴³, oil separation,¹⁴⁴⁻¹⁴⁵ carbon foams,¹⁴⁶ separation of heavy metals,¹⁴⁷ filtration,¹⁴⁸ reaction supports¹⁴⁹⁻¹⁵⁰ and separators in batteries.¹⁵¹⁻¹⁵² Polymerisable emulsions can also be used to produce polymer beads and composites depending on the location of the polymerisable phase as illustrated in Figure 2-14.

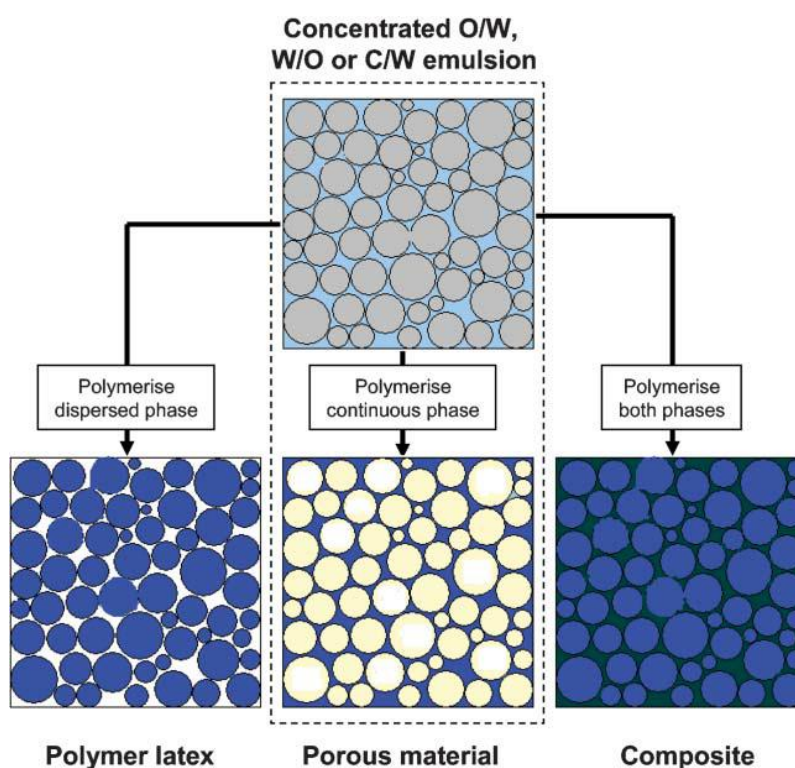


Figure 2-14. Schematic representation of polymerisation of an emulsion in the dispersed phase, continuous phase, and both phases for the preparation of colloids, porous materials, and composites, respectively.¹⁵³

If the dispersed phase of an emulsion is polymerised, solid polymer beads or latexes are produced.¹⁵⁴ Another alternative is the production of composites either by filling the porous structure of the polyHIPE with a polymer solution that is subsequently dried or by simultaneously polymerise monomers in both phases of the emulsion templates.¹⁵⁵⁻¹⁵⁶ A one step approach is also possible, in this case the continuous and dispersed phases are polymerised resulting in the production of composites.¹⁵⁷

2.5.1 Pathways for tuning the morphology of polyHIPEs

The use of emulsion templating allows the possibility to control the morphology of the polymeric materials produced by adjusting several parameters of the emulsions used as templates or the emulsification process itself. The most relevant to this work are discussed below.

Control of polyHIPE morphology by varying the emulsion template composition

The porosity of the templated materials can be easily controlled by varying the amount of internal phase used in the emulsion templates.¹⁵⁸ In the case of pore size and pore throat size, they can be tuned by varying the emulsifiers and the concentration of the emulsifiers used to stabilize the emulsion.^{32, 59} The use of molecular surfactants to stabilize W/O emulsion templates usually results in a porous structure with pores also called in the literature voids,¹⁵⁹ holes, cells⁵⁹ or cavities¹⁵⁴ interconnected by smaller pores, also called interconnecting windows¹⁶⁰ or pore throats¹⁶¹ (Figure 2-15a). In the case porous materials polymerised from solely particle stabilised emulsions, they will typically contain non-interconnected pores after polymerisation as can be seen in Figure 2-15b.^{66, 162}

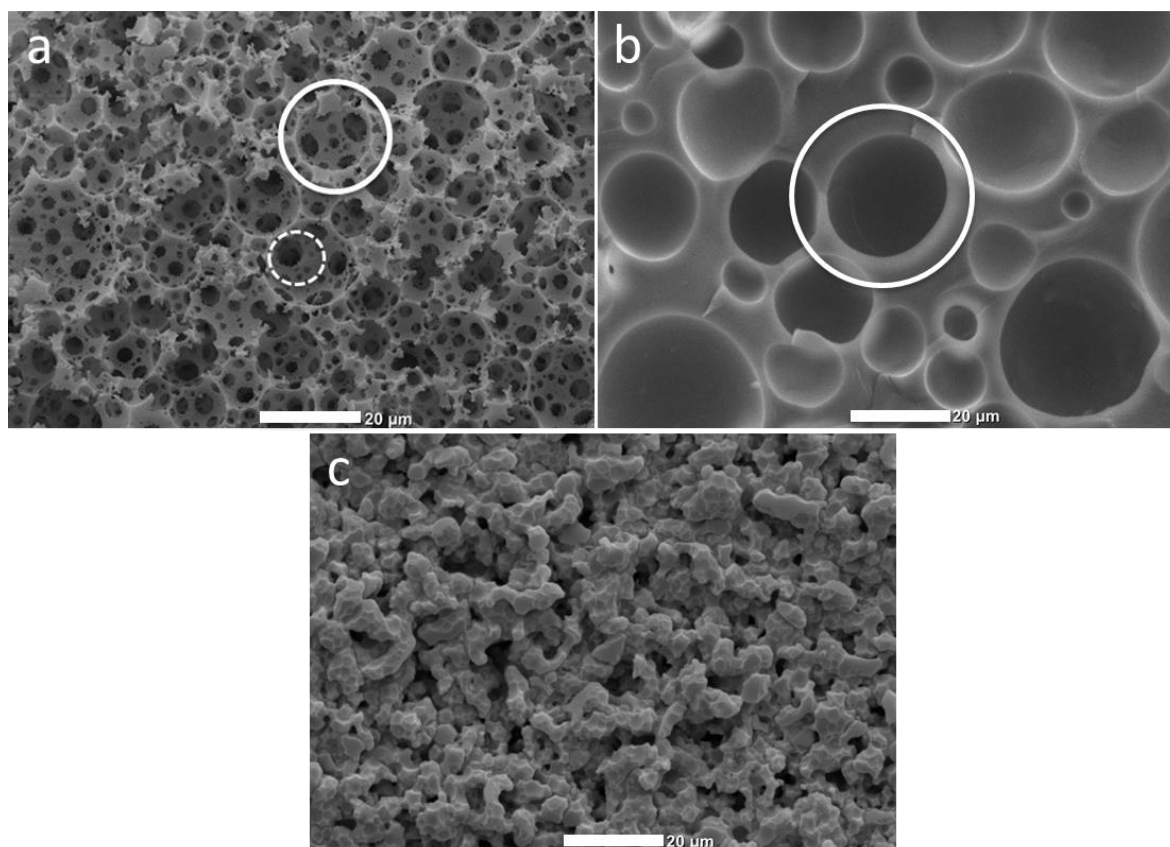


Figure 2-15. Characteristic internal morphology of macroporous polymers obtained after polymerisation of emulsion templates a) polyHIPE synthesised from a surfactant stabilised emulsion. The continuous line indicates the pores formed by the internal phase (template) while the dashed line shows the interconnecting pores b) polyHIPE synthesised from a Pickering emulsion, showing a close celled structure c) polyHIPEs with bi-continuous or non-droplet shaped porous structure

The formation of the interconnectivity in the porous structure of polyHIPEs was studied by Cameron et al.¹⁶⁰ after observing samples taken as the polymerisation of a styrene/DVB HIPEs advanced. The samples were frozen in liquid nitrogen and SEM images taken using cryo-SEM. After analysis, they suggested that the formation of the open cellular structure originated due to density differences in the continuous organic phase arising during polymerisation more precisely between polymer gel phase and monomer phase. As the polymerisation advances, the continuous phase shrinks causing ruptures in the polymer film at the contact point between neighbouring droplets. Later, Menner and Bismarck¹⁶³ after observing the internal structure of polyHIPEs with pores still partially sealed by a thin polymer layer proposed another factor that is believed to influence the formation of interconnecting pores. They believe that pore throats form due to phase separation of the surfactant from the organic phase due to a decrease of the surfactant solubility as the polymerisation advances. This

would drive the surfactant to the oil/water interface in the contact area between neighbouring droplets forming surfactant-rich, polymer poor regions. The post polymerisation processing, where the surfactant is removed and the porous materials dried may cause rupture of thin polymer films formed between pores or enlargement of the existent resulting in an increased interconnectivity. The surfactant concentration in the organic phase plays a key role not only in the formation of stable emulsions but also in determining the final morphology of the porous materials.⁹⁷ Although the optimum concentration of surfactant should be found experimentally, in general stable HIPEs can be created using surfactant concentrations between 0.125 vol.%¹⁶⁴ and 40 vol.%.^{47, 58} The influence of surfactant concentration used to stabilise the emulsion templates in the morphology of the porous material produced after polymerisation was studied by Williams.⁹⁷ It was found that surfactant concentration influenced the pore size, leading to smaller pores with increasing surfactant concentrations. However, if the surfactant concentration is too high, continuity of the polymeric walls was interrupted leading to bi-continuous or non-droplet shaped polymer foams (Figure 2-15c). The excess of surfactant in the emulsion led to porous materials with poor mechanical properties, while a further increase in surfactant concentration created tacky materials unable to support their own weight.⁵⁹ However, the use of surfactant concentrations lower than 5 wt.% does promote the formation of porous materials with a closed-porous structure.⁵⁹

Additionally, average pore and pore throat sizes can be increased by promoting, in a controlled degree, Ostwald ripening of the emulsion templates. Researchers have used organic additives in the internal phase of the emulsions, which after polymerisation, resulted in polyHIPEs with an increase in pore size up to 65 %.¹⁶⁵ Additionally, solvents such as chlorobenzene or toluene were used in the continuous phase of emulsion templates to produce polyHIPEs with reduced pore size and increased pore throat size and surface area.¹⁶⁶ Moreover, the use of non-reactive ingredients (i.e solvent, non-solvent or polymer) diluting the organic phase of emulsion templates was used as common strategy to increase the porosity and surface area of polyHIPEs.¹⁶⁷⁻¹⁶⁸ As the polymerisation advances, since the monomer mixture is miscible with the solvent, but the polymer not, phase separation between the polymer and the solvent occurs. Afterwards, the porogen is removed with the internal phase revealing an additional microporous network within the pore walls complementing the one formed by the dispersed

templating phase. The use of different initiator systems in emulsion templates along controlled coarsening was used to control pore size and pore throat size.¹⁶⁹

The use of an electrolyte in the dispersed phase, such as CaCl_2 or K_2SO_4 , was also found to greatly influence pore size, leading to smaller pores at higher electrolyte concentrations.^{97, 99}

In the case of macroporous polymers from Pickering emulsion templates, pore interconnectivity can be developed by adding small amounts of surfactants to the emulsions after emulsification.^{52, 170} Interconnected polymer foams from particle stabilised HIPEs were obtained by Wong et al.¹⁷¹ by using a combination of surfactant and titania nanoparticles to stabilise the emulsion templates. In these emulsions, different amounts of non-ionic surfactant (Hypermer B246SF) were added simultaneously with the aqueous dispersed phase to the organic continuous phase containing 0.8 to 4.2 wt.% titania nanoparticles. The use of both stabilisers led to emulsions in which water droplets stabilised predominantly by particles or surfactant coexisted. The porous morphology obtained after polymerisation of the emulsion templates presented two distinguishable groups of pore sizes. The bigger pores, typical for polyPickering HIPEs with diameters between 160 and 400 μm and were surrounded by interconnected smaller pores with sizes between 13 and 30 μm .

Use of temperature to influence the morphology of polyHIPEs

It was also shown that the polymerisation temperature can be used to influence pore size distribution without changing the composition of the emulsion used as template;¹⁷² higher polymerisation temperatures accelerated the decomposition rate of the thermal initiator used leading to porous polymers with smaller pores. Additionally, it was demonstrated that pore and pore throat sizes of polyHIPEs can be increased by raising the temperature of the aqueous dispersed phase with before emulsification.¹⁶⁵ In this case, the pore and pore throat sizes of polyHIPEs were increased more than 3 times by increasing the temperature of the aqueous dispersed phase from 23°C to 80°C prior emulsification. Furthermore, the morphology of the porous materials can also be tailored by controlled coalescence, this technique was used by Unilever scientist to control droplet size between a few micrometres and 100 μm to tailor HIPE stability and varying the temperature during emulsification and other emulsification parameters, such as mixing speed and the mixing time.¹⁷³

Control of polyHIPE morphology by varying the energy input during emulsification

By controlling the energy input applied during emulsification, it is possible to modify pore and pore throat sizes⁸² and, therefore, the mechanical properties of the resulting macroporous polymers.²¹ In porous polymers produced by Tebboth et al.¹⁷⁴ after polymerisation of emulsion templates produced with different energy inputs, it was noted that the average pore size decreased with increasing emulsification energy, which was expected due to additional droplet break-up. Furthermore, it was noted that if the energy input applied during emulsification was minimal, larger droplets were produced, leading to larger pore and pore throat sizes after polymerisation of the emulsion templates. However, destabilisation of the emulsion produced was observed, leading to a decrease in the permeability of the macroporous polymers produced.

2.5.2 Tailoring the mechanical properties of polyHIPEs

Depending on the requirements of the application, porous materials with different mechanical properties ranging from brittle, ductile to plastic materials can be desired. For macroporous polymers from emulsion templates, it is possible to tailor the mechanical performance of polyHIPEs by using different monomers in the organic phase of the emulsion.¹⁵³ The characteristic mechanical behaviour of polyHIPEs can be described by a typical stress-strain curve (Figure 2-16) obtained via compression testing.

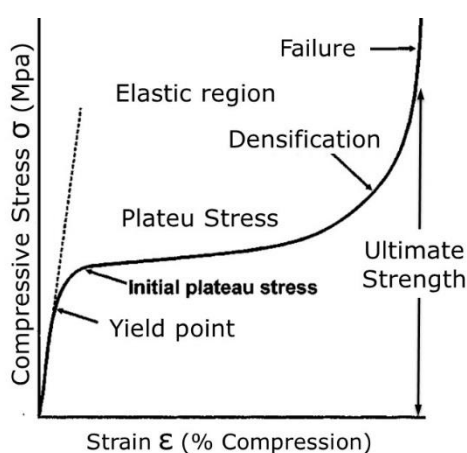


Figure 2-16. Schematic of a typical of stress-strain curve obtained after compression testing of polyHIPEs. Adapted from³²

Compression tests are commonly used for the characterisation of porous polymer materials. At small strains, usually less than 5 %, ¹⁷⁵ an initial linear slope can be observed from which the elastic modulus is determined. The linear region goes up to a yield point, which is characteristic for the maximum load that the original structure can sustain. Above the yield point, the material starts to collapse and behaves plastically, becoming more compacted and not returning to its original length and strength once the load is removed. In this plateau region the pore walls collapse by elastic buckling, plastic yielding or brittle crushing, depending on the mechanical properties of the pore walls. Collapse progresses at roughly constant load, giving a stress plateau. As the load increases, we enter the densification region, here the collapse progresses and the opposing pore walls meet and touch. In this region the stress increases abruptly. Materials are described as brittle when they fail in the elastic region at very low strains. In the case of ductile materials, they can be significantly deformed before they eventually fail. The use of polyHIPEs and macroporous polymers in general has been limited due to their rather poor mechanical performance compared to nonporous polymers, especially in industrial applications. This is caused by the rather low foam density which debilitates their structural integrity. ¹⁷⁶⁻¹⁷⁷ Another disadvantage is the difficulty to predict the mechanical properties of polymer foams which can be important in the development of materials for specific applications. ¹⁷⁵ The most common approaches used to create macroporous materials from emulsion templates with enhanced mechanical properties are reviewed below.

Influence of fillers and reinforcing ingredients in the mechanical properties

The use of reinforcing materials is not new, construction with mud bricks containing straw or dung is one of the oldest and most versatile building techniques used by humans and can be dated back to 8000 BC. ¹⁷⁸ More recently, epoxy resins are reinforced with carbon or natural fibres in order to obtain composite materials with specific properties, such as improved strength and durability. ¹⁷⁹ Additionally, fillers are used in industry to simply reduce costs by substitution of an expensive bulk material by a cheaper constituent. To determine how effective the use of fillers will be, important parameters are not only size and shape of the fillers but also its adsorption capabilities of the enclosing matrix. ¹⁸⁰ There are several examples describing the use of fillers or reinforcing materials in polyHIPEs. The use of organophilic clays in styrene/DVD based emulsions to improve the thermomechanical properties of the matrix

after polymerisation was explored by Lépine et al.¹⁸¹ Also, silica particles were used to improve the mechanical properties of styrene/polyethylene glycol dimethacrylate (PEGDMA) foams.¹²³ Additionally, silylated silica particles in combination with a non-ionic surfactant were used to stabilise W/O emulsion templates based on styrene and PEGDMA.¹⁸² In this case, interconnected macroporous polymers were obtained after polymerisation with a dramatic increase (up to 600 %) in Young's modulus.¹⁸² Emulsion templates stabilised with a surfactant and iron oxide nanoparticles were used to obtain polyHIPEs with magnetic properties and enhanced Young's modulus.^{91, 183} Additionally, carbon nanotubes (CNT) were used as stabilisers of W/O emulsion templates to produce polymer foams with enhanced mechanical and electrical properties.¹⁸⁴

Influence of foam density in the mechanical properties

The capacity of a porous material to withstand compressive forces is strongly related to the density of the material. A route to increase the foam density of polyHIPEs is to polymerise emulsion templates with increased continuous phase volume ratio.¹⁷⁵ When the organic phase ratio is increased, the synthesised macroporous polymers have a higher apparent density, resulting in thicker pore walls and increased Young modulus. Simultaneously, the characteristic interconnectivity of the polyHIPEs or polyMIPEs are still kept.¹⁸⁵ However, modifying the emulsion template formulations can be challenging due to the thermodynamically unstable nature of emulsions and the many parameters involved in the formulation and emulsification process. Emulsions with low and medium internal phase concentrations usually possess a poor stability against sedimentation compared to HIPEs. This is caused by the droplet arrangement in the emulsion resulting in less droplet interaction and a higher sedimentation (W/O) or creaming (O/W) rates compared to HIPEs.⁸³

Influence of the surfactant concentration used to stabilise HIPEs in the mechanical properties

The crush strength of polyHIPEs is influenced by the surfactant concentration used to stabilise the emulsion templates.⁵⁹ This is related to the influence of the surfactant concentration on the emulsion morphology and the resulting pore and pore throat size distribution of the polyHIPEs obtained after polymerisation. These two variables influence the overall ability of the polymer foams to withstand compressive forces. PolyHIPEs with hierarchical pore size

distributions were shown to have a higher crush strength and elastic modulus when compared with materials of similar porosities.^{171, 186}

Furthermore, the plasticising effect of surfactant was observed by Williams⁹⁷ in polyHIPEs containing styrene and DVD in the organic phase. Ceglia et al.¹⁸⁷⁻¹⁸⁸ suggested that the excess of surfactant in the emulsion templates led to the formation of surfactant micelles in the polymer walls. The heterogeneous pore walls formed after polymerisation, which possessed a softer polymer layer near the surface and a harder layer in the bulk, contributed to a reduced elastic modulus of the synthesised polyHIPEs. Therefore, reducing the surfactant concentration in the emulsion can be used as an effective tool to create porous materials capable to withstand higher loads if the surfactant concentration used is sufficient to achieve a stable emulsion.

An alternative to significantly increase the mechanical strength of polyHIPEs was developed by Luo et al.¹⁸⁶ They used RAFT polymerisation to reduce the formation of defects in the polymeric wall producing styrene/DVD polyHIPEs with more homogeneous pore walls. The foams obtained possessed a Young's modulus and crush strength almost 4 times higher than materials synthesised from in situ free radical polymerisation, reaching the theoretical value for polystyrene foams of similar porosity. Based on the results obtained, they proposed that the heterogeneity of the polymeric wall is the main reason causing the low mechanical strength of polyHIPEs.

Influence of crosslinking level in the mechanical properties of polyHIPEs

Another path to modify the mechanical properties of porous materials is to use higher crosslinking levels in the emulsion templates. Most of the experimental work in the literature about mechanical properties of polyHIPEs used styrene and DVB as monomer and crosslinker in the emulsion templates.¹⁸⁹ For this specific system it is known that the Young's modulus increases with increasing crosslinking levels but at the expense of an increased brittleness of the porous polymer produced.⁹⁷ An alternative is the use of a more flexible crosslinker, such as ethylhexyl acrylate (EHA) or polyethylene glycol dimethacrylate (PEGDMA) instead of DVB, resulting in polymers with an increased Young's modulus and controlled brittleness.^{185, 188} The combination of monomer and crosslinker used is determined by the immiscibility of the monomer phase in relation to the dispersed phase.

Influence of emulsification conditions in the mechanical properties of polyHIPEs

The influence of the preparation procedure used to produce the emulsion templates was also determined to play a crucial role in the pore size, pore size distribution and permeability of the polyHIPEs produced.¹⁵¹ It was found by Abbasian et al.¹⁸⁹ that polyHIPEs made from templates where the dispersed internal phase was added more slowly to the emulsion and higher stirring rates were used showed smaller pore sizes and higher compressive properties than those produced using higher dispensing rates. On the other hand, Williams et al.⁹⁷ reported a relatively small influence of the pore size in the Young's modulus of polyHIPEs. However, a clear relation between pore size and mechanical properties is not entirely clear. Certain geometric aspects of the pore morphology are crucial to the understanding of the mechanical properties. Besides the relative density, the anisotropy of the pore structure, influences the mechanical behaviour, the tendency for cells to be elongated, or flattened, or have walls of unequal thickness.¹⁹⁰ These effects become more important for broad pore size distributions where the thickness of the pore walls is not homogeneous. Gibson and Ashby¹⁹¹ stated that for brittle open-cell foams of the same relative density, the crushing strength decreases with increasing cell size. However, values measured showed some variations when compared with the model proposed. These differences were believed to occur as a result of the difficulty to estimate the pre-existing flaw size within the cell wall. The relation between Young's modulus and pore size was studied by Ceglia et al.,¹⁸⁷ showing a decreasing performance in polyHIPEs with smaller pores. Similar results were observed in polyHIPEs synthesised by Huš et al.,¹⁰⁸ where an improvement in mechanical properties was obtained when lower stirring rates (500 rpm compared to 15000 rpm) were used. This improvement was explained by the formation of a more hierarchically developed porous structure. In a later study, it was proposed by Ceglia et al.¹⁶⁵ that the large concentration of surfactant in the emulsion templates led to the formation of surfactant micelles in the polymer walls, this was taken into account and a correction to the model proposed by Gibson and Ashby¹⁹¹ was presented.¹⁹¹ Wong et al.¹⁷¹ observed that a rather broad pore size distribution could originate a more efficient packing of the pores and, therefore, improve mechanical strength despite the presence of pore throats. In a later study, polyHIPEs with an optimised packing configuration were produced, showing an improvement in Young's modulus and crush strength compared with polyHIPEs with a monodisperse pore size distribution.⁴⁹ Additionally, a simulation study was done based on various pore size distributions where it was confirmed the influence of an

optimal packing arrangements. However, these models did not consider the effect of pore throats on the overall mechanical properties. It is apparent that, despite the weakening effects of pore throats, the formation of a hierarchical pore network with an optimum pore packing provides an enhanced resistance to compressive forces.⁴⁹

2.6 Common synthesis techniques of porous polymer beads

A wide variety of approaches for the production of porous and non-porous polymer particles in different sizes and shapes are well documented in the available literature.¹⁹²⁻¹⁹³ The size and size distribution of the beads are usually dictated by the application requirements. For example, beads for chromatography applications should be monodisperse and below 5 μm ,¹⁹⁴ while other applications, such as catalyst supports may need larger bead sizes and in this case the size dispersity is not so important.¹⁸ On the other hand, the synthesis methods chosen will allow for production of beads with a certain size and size distribution. Production methods based on particle nucleation and growth, such as batch emulsion,¹⁹⁵ dispersion¹⁶² and precipitation polymerisations¹⁹⁶⁻¹⁹⁷ are ideal to produce porous and nonporous particles in size ranges from approximately 10 nm to a 10 μm .¹⁹⁸ Due to different uses found in the literature, the term “suspension polymerisation” will be used in this thesis according to the definition provided by IUPAC.¹⁹⁵ Thus, suspension polymerisation is the process defined as a polymerisation in which the initiator is soluble in the monomer, and these two are insoluble in the polymerisation medium (later, this process will be explained in detail). The main difference with the process called emulsion polymerisation, is that in the latter a continuous phase soluble initiator is used, hence the mechanism completely changes. In order to stay oriented with the purpose of this thesis, this literature review will focus on methods capable of producing macroporous beads with diameters ranging from 100 to $\sim 2000 \mu\text{m}$. Production methods, such as suspension, membrane/microchannel and microfluidics polymerisations allow to produce particles with the set dimensions.¹⁹² In this literature review, three heterogeneous polymerisation methods, namely suspension polymerisation, sedimentation polymerisation and microfluidic polymerisation, which are relevant to the experimental work reported in this thesis will be reviewed. Besides particle dimensions, porous beads can be classified according to their internal morphology, pore size and size distribution. The internal morphology and pore size of porous beads is usually determined by the templating method used to produce the particles. According to IUPAC, porous materials can be classified

according to their pore size in micro-, meso-, and macroporous materials with pore sizes of <2, 2–50, and >50 nm, respectively.¹⁶⁷ Occasionally, the term “gigapore” is used in the literature to describe pore sizes >200 nm typical of porous polymers obtained by polymerisation of emulsion templates.¹⁹⁹ While this term is more frequently used in the literature describing chromatography applications,²⁰⁰ it was also used to describe porous particles with a pore-to-particle diameter ratio of $d_{\text{pore}}/d_{\text{particle}} > 0.01$.²⁰¹ While several reviews were written about the various methods available to produce porous particles¹⁹² this review will focus on the production of beads with micrometre sized pores by emulsion templating.

2.6.1 Production of macroporous beads by multiple emulsion templating

Macroporous beads with the desired characteristics can be easily produced by multiple emulsion templating. To produce macroporous beads using this method, a polymerisable W_1/O emulsion is injected into a suitable secondary aqueous phase (W_2) forming a double emulsion (Figure 2-17). After injection of the primary emulsion into the secondary or “carrier” phase (W_2), emulsion droplets are formed.

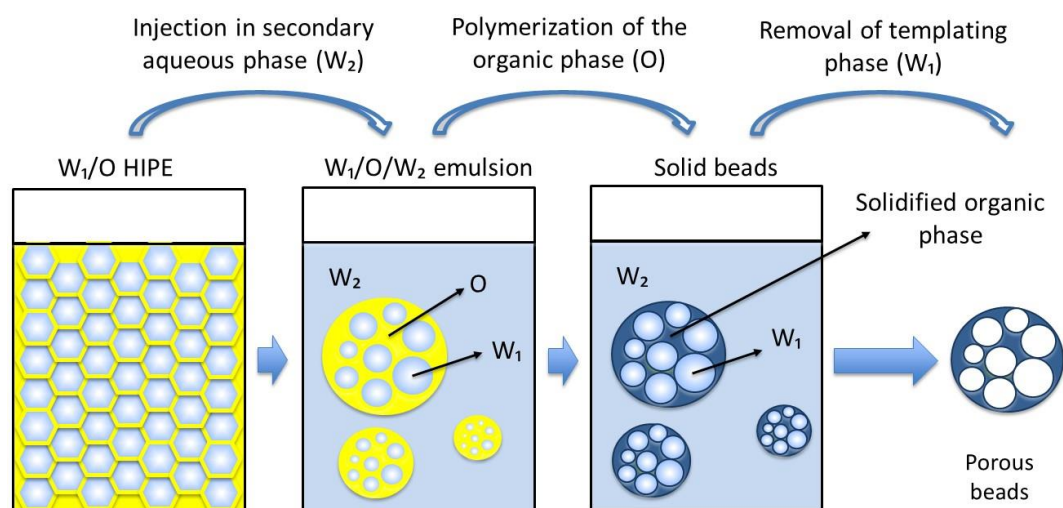


Figure 2-17. Schematic of the production of porous beads through multiple emulsion templating.

Emulsions droplets will always tend to minimise their surface area relative to their volume forming spherical droplets in case of emulsions with a relatively low viscosity.¹⁵³⁻¹⁵⁴ If the viscosity is too high to adapt a spherical lowest-surface-area droplet, an ellipsoidal droplet or rod will form.²⁰² In order to produce solid beads, the organic phase of the droplets is polymerised. Usually, photoinitiation is preferred over thermal initiation, as high

temperatures may promote emulsion destabilisation.²⁰³ The final shape of the beads is determined by the shape of the W_1/O emulsion droplets during polymerisation. After the polymerisation of the emulsion droplets is completed, the solidified beads are separated and collected from the secondary phase (W_2), then the internal templating (W_1) phase is removed resulting in macroporous beads. Also, porous beads without a polymeric wall can be created using colloidal particles dispersed in a solvent as oil phase by jamming or locking of those particles when the solvent is removed.²⁰⁴ Traditional suspension polymerisation and variations, such as sedimentation polymerisation²⁰⁵ are commonly used to produce millimetre sizes porous particles. These production methods, along with the recently developed microfluidic polymerisation are described in the following sections.

2.6.4.1 Synthesis of macroporous beads via suspension polymerisation

Heterogeneous polymerisations, such as suspension polymerisation, sedimentation or microfluidic, are based on the dispersion of one liquid phase into another immiscible liquid phase. Suspension polymerisation is used in industry to produce many important polymers, such as poly(vinyl chloride), poly(methyl methacrylate) and (expandable) polystyrene among others.²⁰⁶ The denomination suspension polymerisation is based on the transition from a liquid/liquid to a solid/liquid system in which the solid particles formed by polymerisation of droplets which are suspended in a continuous liquid media. In a classical suspension polymerisation, energy is applied to the system in order to break the dispersed phase up into discrete droplets by continuous agitation i.e. stirring as shown in Figure 2-18. The dispersed phase is the polymerisable phase containing a mixture of monomers, emulsifiers and initiator while the continuous or secondary phase acts as a polymerisation medium. In suspension polymerisation, the initiator is soluble in the monomer phase and the volume ratio between the monomer phase and the polymerisation medium is usually between 0.1 and 0.5.¹⁹⁸ While thermal initiation is commonly used, other alternatives, such as UV initiation are also possible. A combination of monomers and emulsifiers along with a UV photoinitiator in the monomer phase of a W_1/O emulsion allows the rapid polymerisation of the organic phase forming solid porous beads.²⁰⁷ Moreover, the production of beads by using an aqueous soluble monomer as discrete phase suspended in an oil continuous phase was disclosed in a patent by Dow,²⁰⁸ for the production of polyacrylamide beads with diameters ranging between 75 and 500 μm .

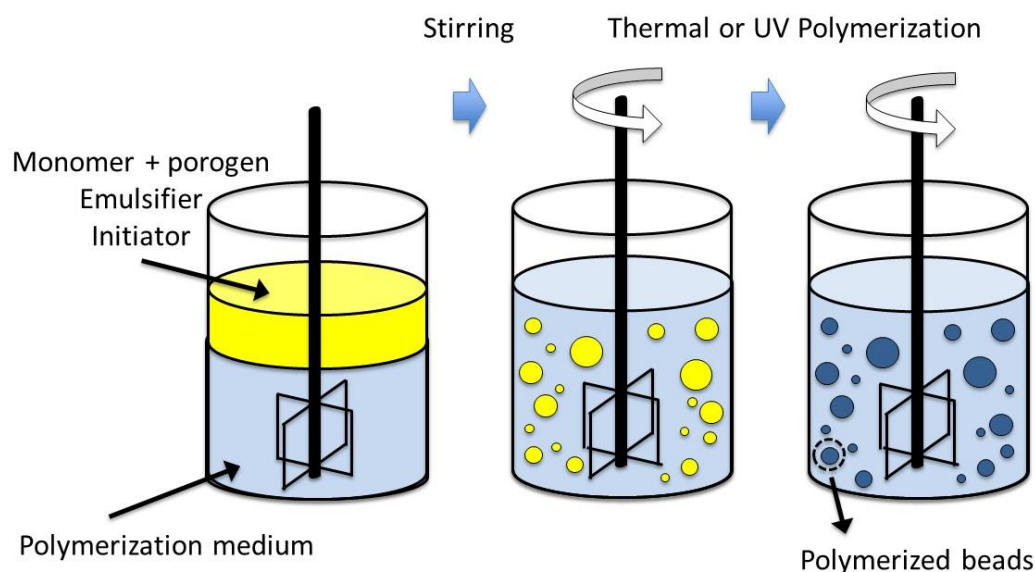


Figure 2-18. Schematic of the suspension polymerisation process for latex production.

In order to create beads with a controlled porosity, it is also possible that the dispersed monomer phase contains an immiscible liquid (forming a multiple emulsion), a solvent or a solid porogen.²⁰⁹ The size and size dispersion of the beads formed will be related to the amount of energy supplied to the system. In classical suspension polymerisation, beads with a size range from 100 nm to about 1-2 mm can be produced.¹⁹⁸ The droplet size and size distribution, which will determine the final size of the beads, can be controlled by varying the stirring speed, which is by far the most convenient parameter to control the particle size.²¹⁰ Also, formulation parameters, such as phase volume ratio between dispersed monomer phase and polymerisation medium, concentration of emulsifiers and the viscosities of both phases influence the particle size. Additionally, setup parameters including the shape of the reactor, the stirrer size and shape influence the dimensions of the beads produced. However, despite the various alternatives to control bead size, the uncontrolled collision and break-up of droplets due to constant agitation inherent to this production system almost always leads to polydisperse particles. Despite the broad bead size distribution, suspension polymerisation is a commonly applied production methods in industry due to its low cost and easy upscaling. In order to meet the particle size range needed for a specific application, the polymer particles produced are sieved after polymerisation and the undesired sizes reprocessed or discarded.

2.6.4.2 Synthesis of macroporous beads via sedimentation polymerisation

A simple but effective method to produce particles in the millimetre range is sedimentation polymerisation. In this technique, proposed by Ruckenstein and Hong,¹⁵⁴ droplets of an aqueous monomer solution were released from a needle connected to a syringe pump into a heated tank filled with an immiscible secondary organic phase. After release, the droplets slowly settled to the bottom of the tank due to gravity. While precipitating, monomer in the droplets started polymerisation, reaching the bottom of the tank partially gelled (Figure 2-19a). The gelled droplets remained at the bottom of the tank for 30-60 min to complete polymerisation. The average size of the droplets was controlled by varying the diameter of the needle used and the injection speed, leading to beads as large as 2.54 mm with a standard deviation of 5.6 % using low injection speeds. The monomer droplets were released individually leading to beads with a narrow size distribution as no collision or agglomeration of droplets occurred during sedimentation. When the injection speed was increased, it was possible to reduce the average size of the beads produced to 0.46 mm but the standard deviation increased to 34 %. The same concept can be applied to create macroporous beads if a W_1/O emulsion is injected into a secondary aqueous phase creating a $W_1/O/W_2$ multiple emulsion template.²¹¹

2.6.4.3 Synthesis of macroporous beads via “in suspension” polymerisation

A variation of sedimentation polymerisation is created by the addition of mechanical stirring of the secondary phase. The modification in the setup can be used to prevent agglomeration of the polymerising droplets, leading to a “in suspension” polymerisation (Figure 2-19b). This technique was used when longer polymerisation times, typical for thermal polymerisation were required.²¹² “In suspension” polymerisation was used to prepare spherical beads with an interconnected pore structure after droplets of a W_1/O HIPE were released into a secondary aqueous solution (W_2). This approach for the production of polymeric microbeads with porosities up to 98 % was disclosed in two patents by Biopore (Biopore Corporation, Los Gatos, USA).²¹³⁻²¹⁴ “In suspension” polymerisation has been used by several researchers to synthesise beads from $O_1/W/O_2$ emulsions. Zhang et al.^{154, 155} used this method for the synthesis of porous inorganic porous beads with average diameters between 1 and 2 mm. After calcination of the polymeric template, porous inorganic beads (silica, Al_2O_3 , TiO_2 , ZrO_2) with a high pore volume ($\sim 6 \text{ cm}^3/\text{g}$) and a surface area of $>400 \text{ m}^2/\text{g}$ were obtained. A similar

“in suspension” polymerisation approach was employed by Desforges et al;²¹⁵ they used $W_1/O/W_2$ multiple emulsion templates for the production of spherical functionalised polyHIPE beads with a diameter between 1 and 3 mm for solid-phase synthesis. To produce the beads, W_1/O emulsions containing ST/DVB as monomer phase were injected into an aqueous solution under continuous stirring forming emulsion droplets. The aqueous solution contained a hydrophilic polymer as a stabiliser. The yield of beads recovered after polymerisation, compared to the volume injected, was claimed to be in the range of 65–95 %. The beads had a broad size distribution. The same technique can be used to produce styrene/DVB/EGDMA porous beads. These beads can be further modified by introducing reactive ester moieties. The beads produced in this case had an average bead size between 50 to 230 μm with a high degree of size dispersity.²¹⁶

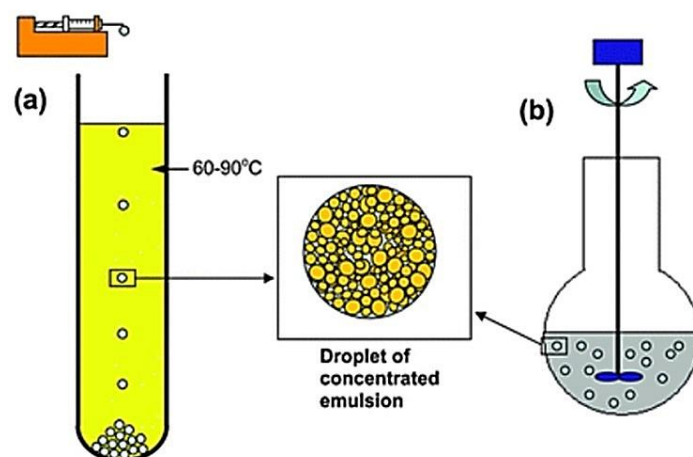


Figure 2-19. Schematic representation of (a) the thermal sedimentation polymerisation method employed by Ruckenstein¹⁵⁴ to produce solid particles by polymerisation of water soluble monomer droplets in a hot oil bath and (b) synthesis of macroporous beads by “in suspension” polymerisation of W/O or O/W emulsion droplets into an immiscible secondary phase creating $W/O/W$ or $O/W/O$ multiple emulsions.¹⁵³

More recently, “in suspension” thermal polymerisation has been used to produce polyHIPE beads by polymerisation of $O/W/O$ Pickering emulsions to be used as photocatalyst support. A TiO_2 nanoparticle stabilised O/W emulsion was produced; the Pickering emulsions were injected into a secondary organic phase at 50°C to polymerise, leading to porous beads with TiO_2 particles on the surface of the polymer walls.¹⁸ Additionally, macroporous beads were produced using this technique after injection and thermal polymerisation of a W/O emulsion

droplets into a secondary aqueous solution.²¹⁷ After post functionalisation with amines, such as 1,4-ethylenediamine (EDA), 1,6-hexamethylenediamine (HMDA) and 4-aminosalicylic acid (ASA), the beads were used for metal adsorption of Ag(I), Cu(II) and Cr(III) ions.

A negative effect repeatedly observed in sedimentation and suspension based approaches is the destabilisation of the emulsion droplets after injection. The combination of high stirring speeds over sustained periods of time and the temperatures needed to initiate thermal polymerisation often lead to destabilisation of the emulsion droplets. The premature destabilisation of the emulsion droplets leads to a reduction in the particle yield thus reducing the efficiency of the process. From different initiation systems that can be used such as thermal, redox, catalytic, UV, or microwave induced initiation, the use of UV initiated polymerisation allows for faster curing of the beads. The reduction of the polymerisation time from several hours to a few minutes along with the lower temperatures used compared with thermal polymerisation are an effective tool to reduce destabilisation of emulsion droplets.²¹⁸

2.6.4.4 Synthesis of macroporous beads via microfluidic polymerisation

An alternative method for the production of particles is through microfluidic polymerisation. The use of microfluidic technologies is based on the manipulation of microflows producing a stream of uniform and evenly spaced droplets with volumes in the picoliter or femtoliter range. Since the droplets are produced individually under identical conditions, a precise control over the droplet size can be achieved. Depending on the microfluidic devices used monodisperse emulsions with a droplet size in the order of a few millimetres²¹⁹ to micrometres²²⁰ or even submicrometre-scale²²¹ were produced. The small scales and flow rates used in microfluidic synthesis allows a continuous operation of the devices in laminar flow. The transition from a laminar to a turbulent flows is calculated using the Reynolds number (Re), which is the ratio of the inertial forces to the viscous forces acting on a small element of fluid and can be calculated by Equation 2-10:

$$Re = \frac{\rho VL}{\mu} \quad \text{Equation 2-10}$$

where μ is the dynamic viscosity, ρ is the density, and V is the average velocity of the fluid and L the diameter of the channel. The Reynolds number for microfluidic devices is typically less

than 1.²²² Laminar flow allow for the production of droplets with a controlled size distribution. A commonly used measure of the size distribution is the coefficient of variation (CV) or size dispersity. This parameter can be defined as the ratio between the standard deviation of the size distribution and the mean droplet size, as presented below in Equation 2-11,

$$CV = \frac{\mu}{\sigma} \quad \text{Equation 2-11}$$

where μ is the mean bead size and σ the standard deviation. A CV below 5 % is commonly accepted as definition of monodispersity.²²³ Usually, for microfluidic devices the is CV in the order of 1-3 %.²²⁴ Besides the production of monodisperse emulsions with controllable droplet sizes and structures,²²⁵ microfluidic techniques can also be used to produce monodisperse porous and non-porous beads.²²⁶

Droplet formation and common geometries used in microfluidic devices

In general, the droplet formation in a microfluidic device can be easily represented as a co-flow geometry as shown in Figure 2-20. An inner fluid is injected or driven into a microchannel through a syringe pump where flow rate or applied pressure are controlled where a second immiscible fluid is circulating driven by another syringe pump. At low flow rates, a constant laminar flow is achieved and when the two flows meet, an emerging droplet starts to grow at the intersection into a spherical droplet. This is the shape with the lowest surface to volume ratio and is governed by the interfacial tension between both phases.

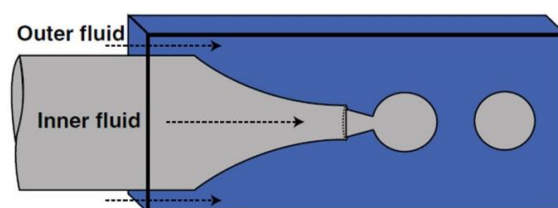


Figure 2-20. Schematic of a co-flow geometry used for the production of droplets.²²⁷

The droplet formation can be represented as a competition between the local fluid stresses that deform the liquid interface and capillary pressure acting to resist deformation. As the droplet grows occupying more space inside the channel, an increase in the upstream pressure is promoted, leading to pinch and detachment of the droplet from the intersection. At this point, discrete and equally sized drops are continuously formed at the tip of the nozzle as

represented in Figure 2-21a, this process is called dripping. After detachment, the droplets are carried by the outer fluid. A different effect denominated jetting occurs at higher flow rates above a critical limit where the inertial forces of the fluid exceed the surface tension forces. In this scenario, no droplet growth and detachment will be promoted and a large jet or stream of inner fluid is formed (Figure 2-21b). At a certain point, the jet breaks in droplets by the continuous phase due to hydrodynamic instability.²²⁸ The droplets are pinched from the jet at irregular time intervals, leading to the formation of droplets with a broad size distribution.

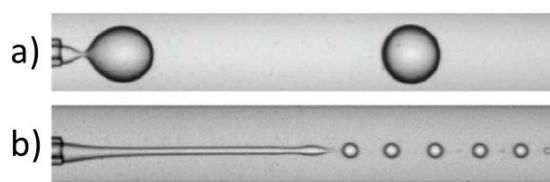


Figure 2-21. Images of drop formation, in both cases the flow rate of the dispersed phase is constant. a) drop formation at low flow rates (dripping regime) and b) jet or stream formed after the flow rate of the inner fluid is increased above the dripping/jetting limit, leading to irregular droplets formation.²²⁹

Different variables, such as the geometry of the intersection and the microchannel dimensions and wettability, the flow rates of the inner and outer phases, polarity difference between the two phases and viscosity of both phases will determine the size and size distribution of the droplets formed.²²⁹ Depending on the flow field in the droplet formation zone, the most common microfluidic geometries can be categorised in three different groups shown in Figure 2-22. First, devices based on co-flowing streams which are the most utilised geometry in microfluidics (Figure 2-22a),²²⁰ then geometries where droplet formation occurs in crossflowing streams or T-junctions (Figure 2-22b) ¹⁵⁷ and finally geometries in which break-up due to elongational flow is used. These geometries are known as flow focusing (Figure 2-22c).^{115, 230} These different geometries can be used alone or combined²³¹ in a wide variety of microfluidic devices. Also, by combining several droplet generating devices in sequence, it is possible to encapsulate in a bigger droplet the droplets generated in previous process stages. Thus, using this technique it is possible to produce double or higher order emulsions encapsulating various droplets of the same or different flows into a larger droplet.

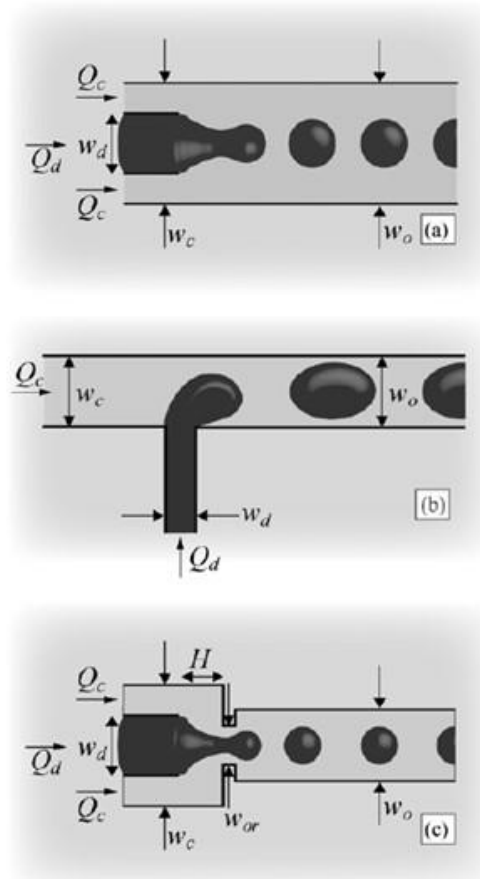


Figure 2-22. Schematic representation of the three main geometries used for droplet production. (a) Co-flow geometries in which inner and outer fluid are injected in the same direction, (b) crossflow or T-junction geometries and (c) stretch or elongational flow in a flow focusing geometry.²²⁴

Microfluidic devices used for the production of porous beads

Microfluidics setups for the production of porous particles¹⁹² as well as the production of droplets and controllable emulsions²³² have been reviewed. Microfluidic devices from silicone rubber poly(dimethylsiloxane) (PDMS) can be fabricated using soft lithography techniques.²²² This technique, developed by Xia and Whitesides²³³ is based on the creation of 2D microchannels into polydimethylsiloxane plates through etching, the process is schematically shown in Figure 2-23. Microfluidic devices containing two-dimensional microchannels offer the advantages of simple fabrication and a clear visualisation of the droplet formation.²³⁴ A further step in this technique, denominated “membrane sandwich” has been used to easily create microchannel networks for production and manipulation of droplets through stacking multiple thin layers of approximately $\sim 100\ \mu\text{m}$.²³⁵ An advantage of PDMS devices is the possibility to seal them reversibly and irreversibly to many materials and be used to encapsulate membranes,²³⁶ microelectronic²³⁷ and optical components.²³⁸ This allows to

produce not only of streams of monodisperse droplets but also complex devices. Although the fabrication of systems in PDMS is relatively simple, microfluidics devices produced from PDMS have a poor resistance to organic solvents and it is difficult to modify the wettability of the microchannels.

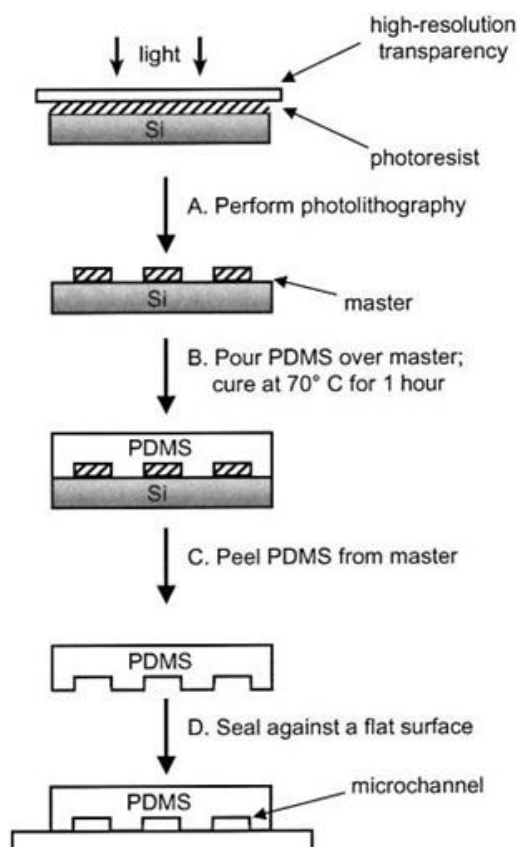


Figure 2-23. Schematic of the preparation process of a PDMS microfluidic device, the entire process requires approximately 24 h.²³⁹

An alternative to PDMS based microfluidic devices is the use of glass capillary microfluidic devices developed by Utada et al.^{19, 240} Devices manufactured using coaxial assemblies of glass capillaries have the advantage of an easily controlled wettability after treatment with appropriate surface modifiers. For example, modification of the glass surface with (octadecyltrimethoxy) silanes renders the device surface hydrophobic, while treatment with 2-[methoxy(polyethyleneoxy)propyl]trimethoxysilane led to an hydrophilic surface. The use of glass capillaries also provides the advantage of easily fabricate three dimensional structures, where a microchannel can cross over or under another. Furthermore, specifically designed capillaries can be used to split single or multiple emulsion droplets, increasing the droplet production rate of the devices while maintaining droplet monodispersity.²⁴¹ In a

typical co-flow capillary device (Figure 2-20), both inner and outer fluid are injected in the same direction. In order to produce droplets smaller than the orifice of the capillary, it is possible to inject the inner and outer fluid in opposite directions (Figure 2-24a). In this case, the inner and outer fluid are collected through the capillary after a jet is formed at the orifice and individual drops are formed farther downstream. Both capillary configurations can be combined in order to create multiple emulsions (Figure 2-24b). In this case, a combination of co-flow and flow focusing approaches are used, the inner fluid (water or oil) is injected from a tapered capillary into another capillary; called collection tube. An immiscible middle fluid is injected surrounding the injection tube and forming a co-flow with the inner fluid. The outer fluid (immiscible with the middle fluid) is injected around the collection tube in the opposite direction hydrodynamically flow focusing the stream formed by the inner and middle fluids. The three fluids are collected in the collection tube forming double emulsion droplets, which consist of the inner fluid surrounded by a layer of the middle fluid carried by the tertiary or outer fluid (W/O/W or O/W/O).

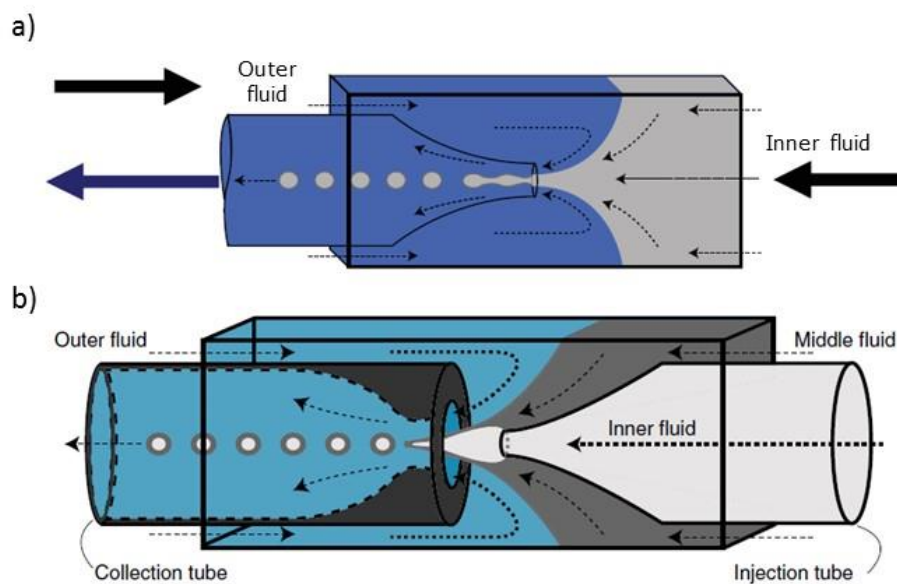


Figure 2-24. Schematic of a) flow focusing geometry where both phases are pumped at constant rates b) Capillary device used to create double emulsions combining co-flow and flow focusing. The arrows point in the direction of flow total flow.²²⁷

Besides the combination of co-flow and flow focusing geometries, multiple emulsions can be obtained by using a microfluidic devices consisting of integrated T-junction geometries (Figure 2-25). This geometry was employed by Okushima et al.¹¹⁵ to produce a microfluidic device for

preparing $W_1/O/W_2$ and $O_1/W/O_2$ double emulsions. The devices were prepared by isotropic etching of Pirex glass or by machining of quartz glass. In this case, wetting of the microchannels plays a significant role, in order to disperse aqueous droplets in an organic phase, hydrophobic channels are desirable while hydrophilic microchannels are better suited to disperse organic phase droplets into an aqueous phase. The glass devices were modified to be hydrophobic by using a silane-coupling agent. In this device, the size and amount of the droplets and enclosed droplets was adjusted by controlling the break-up ratio at the two junctions by varying the flow conditions. The size of the droplets produced could be varied from 220 to 95 μm with CVs ranging from 2.6 to 7.1 %.

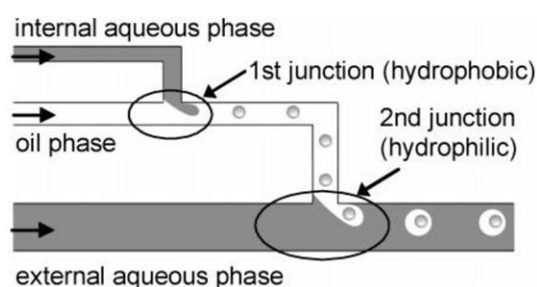


Figure 2-25. Schematic representation of a setup used to prepare double emulsions using T-junction geometries.¹¹⁵

Microfluidic devices can be used to produce double or higher order emulsions by combining several geometries in a sequence. Complex devices with several single emulsification points allow an independent control of the amount and size of droplets to be encapsulated in each phase by adjusting the flow rates used and the geometric dimensions. Complex microfluidic devices can be created from simple building blocks (Figure 2-26a). In this case, three basic building blocks were used to create an adaptable technique that allows for the production of high order multiple emulsions (Figure 2-26b). The basic components were a “drop maker” designed to generate droplets, a connector used to combine droplets created in different drop makers and a liquid extractor used to control the amount of continuous phase in the system. A precise control of the droplet size (D_1) and amount of droplets encapsulated can be achieved by adjusting the flow rates or the inner diameter of the liquid extractor. An important feature of this setup is the possibility to generate multiple emulsions with different fluids (oil or water) as the outermost phase without the need to modify the wettability of the microchannels.

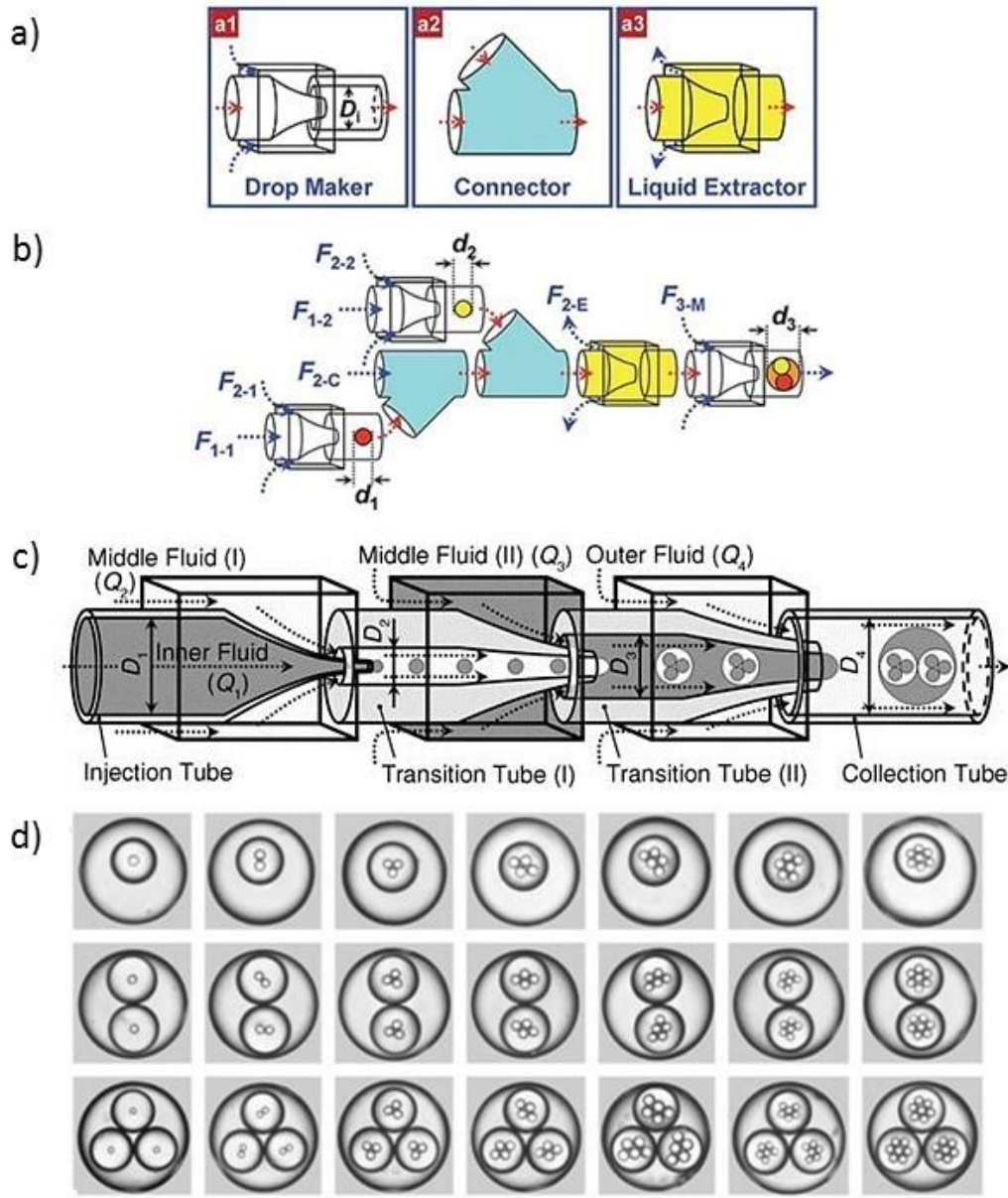


Figure 2-26. a) Schematic representation of basic components used in the microfluidic device²⁴² b) Schematic of the microfluidic device produced using the basic building blocks, which was used to produce quadruple component multiple emulsions.²⁴² c) Schematic representation of multiple co-flow microfluidic device based in glass capillaries used to generate monodisperse triple emulsions.²⁴³ d) Optical micrographs of single, double and triple emulsions that contain a controlled number of droplets of a single component.²⁴³ The scale bar represents 200 μm .

Thanks to the adaptable and scalable setup, it was possible to generate monodisperse multiple emulsion of orders high as sextuple-component triple emulsions while working in a dripping regime.²⁴² A common approach to create high order multiple emulsions is the use of coaxial, co-flow geometries as shown in Figure 2-26c. This kind of setup was employed by Chu et al.²⁴³ for the production of multiple emulsions consisting of several cylindrical glass

capillaries with tapered ends, which were aligned and centred within larger squared capillaries. This microfluidic configuration had the advantage of being easily extended by adding further components in order to produce higher order multiple emulsions. On the other hand, alignment and fitting of the capillaries can be difficult and time consuming. In order to fit the capillaries, the outside diameter of the cylindrical tubes had to match the distance between the walls of the square ones. The cylindrical tubes had a tapered end that is inserted into the next component, in this case a cylindrical transition tube (I) with an internal diameter D_2 . The transition tube (I) was simultaneously introduced into another transition tube (II) with an internal diameter D_3 . The end of the transition tube (II) was inserted into an aligned cylindrical collection tube with an internal diameter D_4 . This device was used to produce $W_1/O_2/W_3/O_4$ emulsion droplets. A single emulsion was formed when droplets of the inner fluid were emulsified by coaxial flow of the middle fluid (I) injected in the square capillary. The emulsion droplets were formed inside the transition tube (I) and were emulsified one more time in the middle fluid (II), which was injected as outer fluid inside the transition tube (II). The flow rates of all fluids in the system were controlled to work in a dripping regime promoting the formation of monodisperse droplets. The droplet size in coaxial flows working in a dripping regime is inversely proportional to the velocity of the surrounding flow,²⁴⁴ this relation was used to control the emulsification process by adjusting the individual flow rates (Q_1 , Q_2 , and Q_3). Additionally, the dimensions of the device were used to control the size and number of the innermost droplets as shown in Figure 2-26d. In this case, the coefficient of variation (CV) of inner and outer droplets in multiple emulsions was $\sim 2\%$. It is also worth mentioning that coaxial microfluidic devices are not as sensitive to the wettability of the glass walls as devices based on T-junction geometries. Therefore, no surface modification is needed, allowing the production of either W/O/W or O/W/O multiple emulsions in the same device.

Simple microfluidic devices based on commercial tubing and needles

The production of complex microfluidic devices based in PDMS or silicon/glass often requires the use of expensive materials or complex assembly techniques and can be easily obstructed by polymer debris.^{223, 245} A simple alternative for the production of microfluidic devices useful for the synthesis of polymer particles is the use of needles and laboratory tubing that act as microchannels. A microfluidic device designed by Quevedo and McQuade²⁴⁶ (Figure 2-27a) was built based in this concept using PVC tubing with an internal diameter (I.D.) of 1.6 mm. In

this case, droplets were formed after injecting an immiscible organic solution using a straight needle with an I.D. of 0.16 mm at a flow rate of 0.141 cm³/min. The needle was injected straight through the tubing forming a crossflow geometry (Figure 2-27b). By controlling the flow rate of the outer aqueous phase and using UV initiated polymerisation of the organic phase, polymer particles with diameters between 320 and 860 µm were produced with a CV between 3.5 and ~8 %, respectively. An advantage of this kind of setup compared with capillary or PDMS devices was the rather quick solution to address issues of clogging by simply replacing the tubing used.

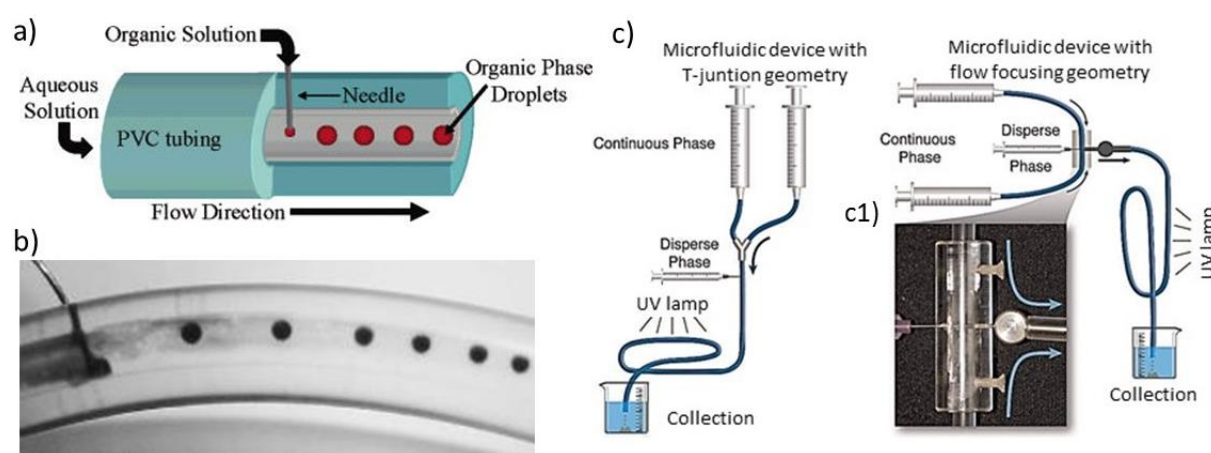


Figure 2-27. a) and b) Schematic and photograph of the crossflow geometry used for the production of polymer particles by Quevedo et al.²⁴⁶, the spherical droplets formed can be seen. c) Schematic representation of a T-junction and flow focusing devices produced using commercial needles, in both cases the formed acrylate droplets are UV polymerised inside the tubing.²¹⁹

An adaptation of the microfluidic device based on PVC tubing and commercial needles was used by Steinbacher and McQuade²¹⁹ for the production of particles with diameters ranging from 25 to 1200 µm with low size dispersion. This setup was built using a T-junction or a flow focusing geometry (shown in Figure 2-27c). The alignment of the tubing and needles in the flow focusing geometry was achieved by using a machined polycarbonate jig (Figure 2-27c1). Both configurations were used to produce microparticles after polymerisation of a dispersed organic (acrylate) phase and presented coefficients of variation (CV) between 5 and less than 1 %. The droplet size and, therefore, the size of the solid beads, was controlled by changing the flow rate of the continuous aqueous phase. The maximum flow rate of the dispersed phase was 2.0 cm³/min resulting in the production of particles with diameters ~200 µm. Under jetting conditions, the system produced droplets with a CV in the range of 10 % to 15 % due

to the formation satellite droplets. While this device was used with a low viscosity organic phase as dispersed phase, an improved version was used by Gokmen et al.^{202, 247} to produce macroporous polymer beads and rods from HIPEs. In their setup, droplets were generated in a co-flow geometry after a W/O HIPE was injected into a circulating aqueous solution (Figure 2-28a), thereby creating a W/O/W system. Spherical beads with diameters around 400 μm were synthesised through the downstream UV polymerisation of the monomers within the individual droplets. Unlike the previous setup, a co-flow geometry was produced by bending 90° the needle used to inject the emulsion into the tubing. The tubing material used was flexible Tygon tubing (the tubing material was not specified) instead of PTFE tubing to minimise leakage in the system. Through an increase in the viscosity of the emulsion and the flow rates used, rods instead of spherical beads were produced. Upon reaching jetting conditions a thread of emulsion formed at the tip of the needle due to the high viscosity of the HIPE and broke into small HIPE segments similar to sausages, which were unable to form spherical droplets after released. The segments formed became macroporous rods after polymerisation. A similar approach, using a HIPE as dispersed phase was employed by Moglia et al.³⁴ for the production of macroporous beads with controllable particle sizes in the range of 200 – 800 μm (Figure 2-28b). The size of the beads produced using this setup was controlled by varying the flow rates of the injected HIPE, the external phase, the needle size and the I.D of the tubing used. Smaller beads with average diameters between 200 and 300 μm were produced using a 0.8 mm I.D. Tygon tubing and HIPE injection rates of 1 mL/h, the maximum flow rate used. All beads produced presented a size standard deviation between 3 and 21 %. More recently, a microfluidic device based on a flow focusing geometry was used by Lapierre et al.²⁴⁸ to produce macroporous beads by polymerisation of HIPEs. The setup was entirely based on polypropylene pipette tips combined with PTFE and silicon tubing held together with a commercially available self-setting silicon rubber (Figure 2-28c). When the rubber is exposed to air, the material cures in approximately 30 min forming a cured flexible silicone rubber that maintains the given shape. After the rubber was moulded, the device could be fabricated in 10 min. This setup was used to produce monodisperse emulsions with a droplet size between 100 and 500 μm controlled by the I.D. of the tubing used. Also, monodisperse porous beads with a diameter of 200 μm were synthesised from an acrylate based HIPE. The spherical polymer beads were fabricated after injecting the HIPE into an oil continuous phase followed by photopolymerisation downstream. The beads produced possessed a high porosity (up to

95 %) and pore sizes ranging from 5 to 30 μm . It is worth mentioning that the PTFE tubing used was hydrophobic thus suited for the W/O HIPEs. The same device was used for O/W emulsions but in this case the tubing had to be replaced with an appropriate hydrophilic glass capillary.

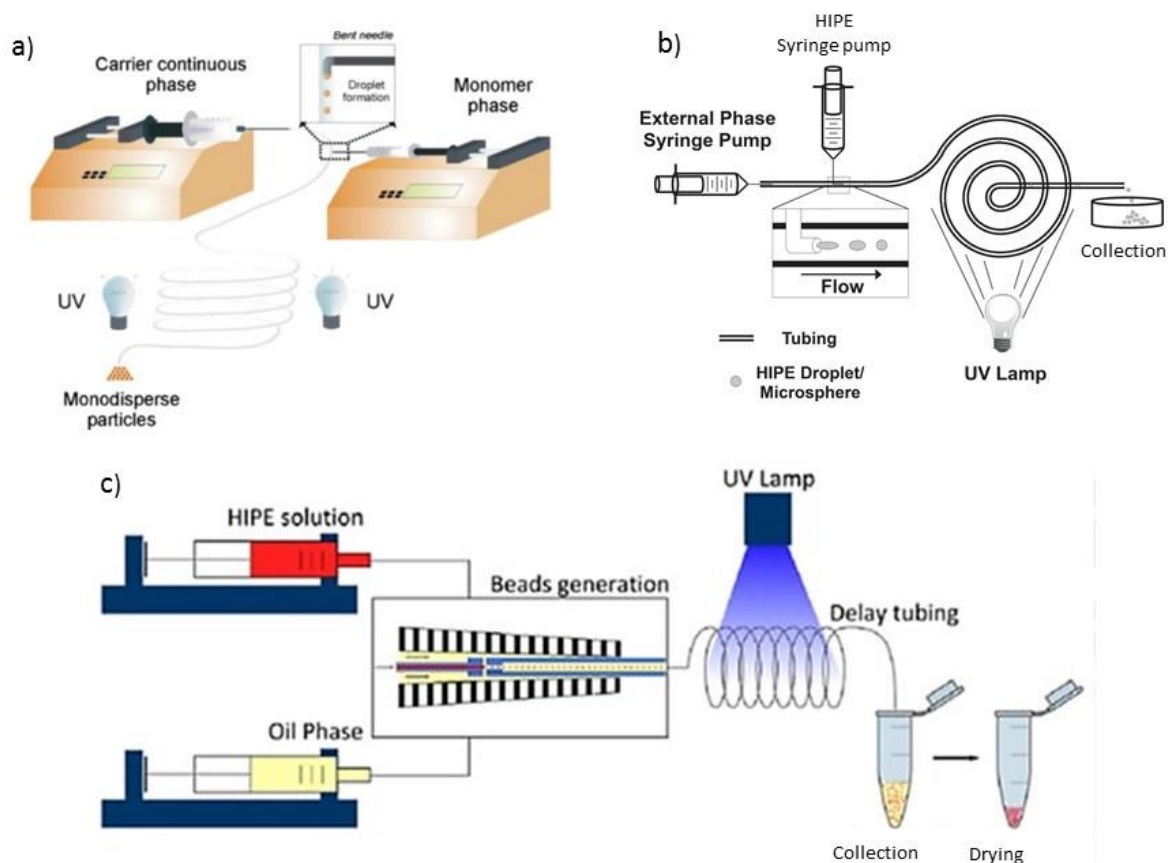


Figure 2-28. a) Microfluidic setup used by Gokmen et al.²⁰² for the production of polymer beads and rods by polymerisation of HIPE droplets using a co-flow geometry b) Schematic representation of the setup used by Moglia et al.³⁴ for the production of polyHIPE beads loaded with a growth factor for controlled release c) Design of a pipette tip based microfluidic setup, the droplets formed were UV polymerised inside the tubing and then collected.²⁴⁸

One of the major disadvantages of microfluidic devices are the low production rates caused by the characteristic small volumes and flow rates used. When HIPEs are used as discrete phase, too high flow rates result in a large thread of emulsion that may eventually obstruct the tubing used leading to clogging. In order to avoid the jetting regime, low flow rates are used which are the major disadvantage as low flow rates led to poor productivity. One of the options to increase the production rate is the parallelisation of devices. Microfluidic devices made from PDMS containing 15 parallelised geometries were used to produce W/O/W multiple emulsions based on sodium alginate, 1-octanol and an aqueous PVA solution as

components. In this case, it was necessary to hydrophobise the device microchannels prior to the experiment. The emulsion production rates obtained were as high as 1 kg/day with a droplet size of 150 μm and a size coefficient of variation (CV) of 6 % using flow rates of $\sim 30 \text{ cm}^3/\text{h}$.²⁰ The same concept could however be problematic when aiming to produce macroporous beads by polymerisation of HIPEs due to their characteristic high viscosity which can lead to clogging of the PDMS microfluidic devices.²⁴⁹⁻²⁵⁰

2.7 Encapsulation of active ingredients in multiple emulsions

Multiple emulsions can be used as versatile carriers for a wide range of compounds due to their multi-compartment structure. A major advantage of microfluidic techniques is the possibility to compartmentalise liquids or active ingredients within droplets through the production of double, triple, and even higher order emulsions, where the volume and amount of the droplets can be precisely controlled. This can be achieved because the liquid/liquid interface acts as a membrane encapsulating the active ingredients inside the droplets.²⁵¹ For example, encapsulation in multiple emulsions can be used to prevent loss of quality due to undesirable release of flavour compounds during processing or storage if the active ingredient is present in the dispersed phase of the emulsion (W_1).²⁵² $W_1/O/W_2$ double emulsions can be used to encapsulate water-soluble molecules or active ingredients in the dispersed aqueous phase (W_1).²⁵³ Additionally, it is also possible to encapsulate active ingredients or oil-soluble molecules in the organic phase of emulsions.²⁵⁴ Encapsulation can be also used to compartmentalise incompatible reagents, such as acids and bases in the same emulsion system.¹¹⁰ This kind of compartmentalisation makes them ideal for controlled release applications of a loaded compound at a controlled rate or in response to environmental conditions, protection of encapsulated sensitive compounds from chemical reactions, bioavailability enhancement, and enzyme immobilisation but also to mask unpleasant tastes in pharmaceutical and food applications.²⁵⁵⁻²⁵⁶ One drawback to achieve efficient encapsulation of an active ingredient inside a multiple emulsion is the diffusion of the active ingredient to the external phase across the interface. This effect, driven by the concentration gradient between two phases of the same nature (for example, W_1 and W_2 in $W_1/O/W_2$ multiple emulsions) can lead to poor encapsulation efficiency and destabilisation of the emulsions.²⁵⁷ Diffusion of entrapped agents, such as hydrochloric acid (HCl) and sodium hypochlorite (liquid bleach) in $W_1/O/W_2$ multiple emulsions, was investigated by Dunstan and

Fletcher.²⁵⁸ They measured the trapping time of a water and dodecane HIPE containing 5 mM HCl in the inner water droplets (W_1). In this case, for HIPEs with approximately constant water droplet size, increasing the oil volume fraction resulted in an increased oil film thickness and, therefore, longer trapping times were obtained. Also coalescence of the inner droplets with the outer aqueous phase (W_2) and breakup of the organic phase (O) can cause losses of the encapsulated substance.²⁵⁹ Diffusion and coalescence among other process parameters are influenced by shear stress during emulsification, the characteristics of the emulsifier used and structural parameters of the emulsion, such as droplet size and internal phase volume ratio.²⁶⁰ Much of the recent work in multiple emulsions has been oriented not only to improve the stability of the emulsions but also to obtain a better control of the release rates of encapsulated ingredients. Some of the most recent achievements focus on the identification of the most suitable emulsifier,^{106, 108, 261} proposing the use of macromolecular emulsifiers for stabilising double emulsions instead of short chain emulsifiers.²⁶⁰ Also significant progress has been made in controlling the droplet size during fabrication of multiple emulsions using microscale systems, such as membranes, microchannel emulsification,²³⁴ and several microfluidic emulsification devices.^{115, 220}

2.8 Encapsulation of active ingredients in macroporous beads produced by polymerisation of multiple emulsion templates

Particles with encapsulated ingredients can be useful delivery systems for controlled (slow and prolonged) release of active ingredients, such as drugs and nutrients in medicine and food industry. It is possible to produce solid particulate delivery systems by polymerising the external organic phase of multiple emulsion droplets ($W_1/O/W_2$). This objective can be achieved in two different ways; the ingredient is already present in the inner droplets of the multiple emulsion (W_1). If the external organic phase containing or consisting of monomers of the emulsion is polymerised, the active ingredient will remain encapsulated inside the solidified particle. In this scenario, the pores inside the solid particles should not be interconnected and the surface should be dense in order to achieve an efficient encapsulation. Another alternative is using multiple emulsions to produce porous particles with an open, interconnected pore structure that can be post-filled with the active ingredient after the particle is formed in order to render it reactive.^{86, 183} However, this post filling technique requires an additional sealing step after the particle are filled with the active ingredient to

avoid dispersion or leaking. Particles synthesised from $W_1/O/W_2$ multiple emulsions can be used to encapsulate water soluble compounds if they are present in the dispersed phase (W_1) of $W_1/O/W_2$ multiple emulsions before polymerisation.²⁶² This technique was also employed by Moglia and Cosgriff-Hernandez³⁴ to synthesise polyHIPE beads from $W_1/O/W_2$ multiple emulsions containing multi-functional growth factors (rhBMP-2, a bone morphogenetic protein) that promote bone regeneration. Additionally, encapsulation of active ingredients is possible if the active ingredient is used to stabilise the W_1/O emulsion templates.⁶⁸ Also, encapsulation is possible if the active ingredients are located at the interface stabilising the W_1/O emulsion.^{68, 263} or in the bulk phase (O).²⁶⁴ Lipophilic compounds, such as essential oils, vitamins, fatty acids or flavours are difficult to deliver in food matrices due to their limited solubility and degradation during physiological transport. Encapsulation of these compounds in solid microparticles and controlled release under specific conditions (e.g. swelling or erosion) is interesting for food, pharmaceutical and personal care applications if the release is activated by various triggers, such as body temperature, intestinal pH or respond to gastric enzymes.²⁶⁴

2.8.1 Alternatives to increase encapsulation efficiency of active ingredients in macroporous beads produced by emulsion templating

Usually, the active ingredients to be encapsulated have a significant economic value. Therefore, in addition to an effective response to release conditions, beads should be able to efficiently encapsulate and provide protection of the active ingredient.²⁶⁵ This condition requires to contain the encapsulated active ingredient at a constant concentration over storage time inside the beads after exposure to different environments. In order to reduce diffusion or loss of the active ingredients, different approaches can be used. A first alternative is the already mentioned increase of the continuous phase volume ratio in the multiple emulsion to prevent diffusion of the encapsulated active ingredients before polymerisation. Also, rapid curing of the interface, i.e using UV polymerisation, can be used to maintain the initial concentration of the active ingredient. Additionally, it was observed by Kim et al.²⁶² a significant influence of the degree of crosslinking in the continuous organic phase of emulsion templates in the release ratio of encapsulated ingredients in PMMA microcapsules. In their work, an increasing encapsulation efficiency was related to a higher degree of crosslinking. Beads were synthesised from emulsion templates containing MMA and EGDMA as monomer

and crosslinker in the continuous organic phase. The beads were able to contain an encapsulated salt after immersion in water for several days and the best results were obtained with a degree of crosslinking between 30 and 50 wt.%. This is due to the formation of a small polymer network that prevents diffusion of the active ingredient out of the beads. For that reason, in this thesis the amount of crosslinker was kept constant at 40 % with respect to the monomer volume in all emulsion formulations. An alternative to avoid diffusion or degradation of the active ingredient encapsulated after polymerisation, is the formation of a non-porous protective layer or “skin” on the surface of the beads. The formation of the “skin” on the surface of macroporous particles synthesised from emulsion templates has been reported several times.²⁶⁶⁻²⁶⁹ Depending on the application of the beads, the formation of a polymer layer or “skin” on the surface can be considered to be very problematic. This is due to the limited number of molecules that are able to permeate through the particle surface and reach the interior of the beads. But in the case of beads already containing an encapsulated ingredient this effect can be used to encapsulate a higher payload. The formation of a smooth “skin” was observed during the synthesis of macroporous polymer beads by the copolymerisation of styrene, (chloromethyl) styrene and divinylbenzene dissolved in 4-methyl-2-pentanol.²⁷⁰ In this case, a polymer layer was observed around beads with a divinylbenzene concentration from 4 to 75 %. The “skin” formation was studied by Dubinsky and Kumacheva²⁷¹ in the production of porous poly(GMA-EGDMA) particles in a PDMS microfluidic device. In their work, it was hypothesised that the “skin” was formed when the interfacial tension between the aqueous continuous phase and the monomer-solvent phase was higher than the interfacial tension between the polymer and the continuous phase. Under those conditions, the interface is deprived of the monomer-solvent mixture, which is expelled to the interior of the bead. In order to prevent the formation of a skin, they reduced the interfacial tension between the monomer mixture and the aqueous continuous phase (2.5 wt.% aqueous solution of PVA) by adding the surfactant t-octylphenoxypolyethoxyethanol (Triton X-100) and also the solvent THF. Also the formation of the protective layer was suppressed by adding the solvent dioctyl phthalate (DOP) to the monomer mixture. Beads synthesised from $W_1/O/W_2$ multiple emulsions containing MMA and EGDMA in the organic phase as monomer and crosslinker were also used to encapsulate a water-soluble ingredient dissolved in the inner aqueous phase of the emulsion (W_1).²⁶² In this case, the active ingredient used was monosodium phosphate (MSP) at a concentration of 3.3 wt.%. The porous particles

were obtained using a “in suspension” thermal polymerisation conducted at 60°C for 10 h. The amount of MSP present in the multiple emulsion was determined to be about 95 %. After polymerisation, solid particles with a size in the range of 100-250 μm were obtained and the loading yield of MSP was determined using conductivity analysis. The encapsulation efficiency was calculated by comparing the loading amount from the weight fraction in the recipe. In the case of non-crosslinked beads, no significant amounts of MSP was encapsulated. On the other hand, beads crosslinked with 10 to 50 wt.% EGDMA had encapsulation yields of 20-50 %. The poor encapsulation rates obtained indicate that a part of MSP ended up in the secondary aqueous phase during polymerisation.

A viable alternative to reduce the permeability of the polymeric walls in porous beads produced by polymerisation of emulsion templates is the use of particle stabilised or Pickering emulsions.²⁷² In contrast to molecular surfactants, porous materials obtained from Pickering emulsions tend to form larger pores. At the time of polymerisation, film ruptures are less likely to occur, leading to a non-permeable or closed-cell structures.^{64, 184} One of the main restrictions in the production of beads from multiple Pickering emulsions using microfluidic devices is the high viscosity of this kind of emulsions.²⁷³ Previous experience in our research group with the production of beads combining multiple Pickering emulsions and tubing based microfluidic devices was not entirely successful due to clogging of the needles used for injection. During injection jetting occurred, leading to the formation of polydisperse non-spherical droplets causing downstream obstruction of the tubing used. The typical viscosity of Pickering emulsions made difficult the transition to spherical droplets, leading to non-uniform beads after polymerisation.

2.9 Summary

The use of multiple emulsions as encapsulation and delivery systems is under constant development, driven by large industries, such as food and pharmaceutical companies, who are pushed by the constant need to develop more efficient products or develop new ones. A major challenge in the application of multiple emulsions is their inherent instability and the low encapsulation efficiency because of diffusion of the encapsulated active ingredients into the surrounding continuous phase. Additionally, $W_1/O/W_2$ multiple emulsions can be used to produce porous beads by polymerisation of the oil phase of the multiple emulsion. However, techniques available to produce large amounts of micrometre sized porous beads face two

major challenges, which are the poor control of size dispersion in case of suspension polymerisation and the low production rates in case of microfluidic polymerisation. The possibility to develop a synthesis alternative for the production of porous beads that combines the advantages of both mentioned production methods presents an interesting challenge. Furthermore, the possibility of using polymerisable multiple emulsions with in-situ encapsulated ingredients to create efficient delivery systems is more than appealing.^{34, 274}

Some of the challenges faced during this thesis included the need to:

- Understand the stability and rheological behaviour of the emulsion templates used.
- To explore new perspectives to the use of emulsion templating as a tool to create efficient delivery systems.
- Develop alternative production methods for macroporous beads that allow control of bead size and size dispersion with high production rates.

Chapter 3. Methodology

3.1 Materials

The monomer methyl methacrylate (MMA), the crosslinker ethylene glycol dimethacrylate (EGDMA), calcium chloride dihydrate ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$) and the emulsifiers poly(vinyl alcohol) (PVA) with an average molecular weight of 30.000-70.000 g/mol, poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) molecular weight of 2.800 g/mol commercially available as Pluronic L-81 and octylphenol ethoxylate (Triton X-405) were purchased from Sigma-Aldrich (Vienna, Austria). The surfactants Hypermer B246 and Cithrol DPHS (formerly known as Arlacel P135) were courteously provided by Croda (Croda GmbH, Nettetal, Germany). The photoinitiator 2-hydroxy-2-methyl-1-phenyl-1-propanone (Darocur 1173) was kindly provided by BTC Europe GmbH (Düsseldorf, Germany).

3.2 Preparation of emulsion templates

The organic continuous phase of all emulsions prepared consisted of a mixture of MMA and EGDMA as monomer and crosslinker (volume ratio of 60/40 %, respectively) mixed with different amounts of the surfactant Pluronic L-81, and the photoinitiator Darocur 1173. Various amounts of an aqueous solution containing 1.3 wt.% (13.2 g/L) of calcium chloride ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$) as electrolyte were used as internal dispersed phase. To prepare the emulsions, the oil continuous phase was mixed in a reaction vessel (glass, 250 ml volume) fitted with a glass paddle rod (2 blades, anchor shape) connected to an overhead stirrer (Heidolph RZR 2102 Control, Heidolph Instruments GmbH, Schwabach, Germany) for 5 min at 500 rpm. After mixing the continuous phase, the aqueous internal phase was added dropwise keeping the stirring speed at 500 rpm. After the internal phase was added, stirring continued at a constant speed for another 5 min, unless otherwise indicated, to produce a homogeneous emulsion. The total volume of continuous and dispersed phase combined was kept constant at 50 ml in order to introduce a similar emulsification energy into all formulations. In the case of multiple emulsion templates ($W_1/O/W_2$), the secondary aqueous phase (W_2) was obtained by dissolving various amount of calcium chloride ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$) in distilled water. The salt concentration in each electrolyte is indicated in the relevant chapter. The aqueous solutions

containing Triton X-405 and polyvinyl alcohol (PVA) were produced by dissolving both components in distilled water at 75°C under constant stirring. After the components were dissolved, the solution was cooled down. It is worth mentioning that no precipitation was observed. Then, the aqueous solutions were stored until use in a closed beaker and stored in a lab refrigerator at 6°C to avoid development of microorganisms.

3.3 Characterization of the emulsion templates produced

3.3.1 Emulsion stability

After preparation, the emulsions were transferred into 50 ml free standing polypropylene centrifuge tubes (LLG GmbH, Meckenheim, Germany). During pouring, the flow behaviour of the emulsions was classified. Once filled, the centrifuge tubes were sealed with Parafilm and stored inside a closed solvent cabinet to avoid exposure to light. In order to characterise the emulsion stability and prevent undesired polymerization, the emulsions were prepared without photoinitiator. The emulsion stability was assessed by visual observation at regular intervals until signs of destabilization such as sedimentation or coalescence were observed, this point was considered the beginning of phase separation.

3.3.2 Energy input during emulsification

The energy used during the emulsification process was calculated as follows;

$$E_v = \frac{Pt}{V} \quad \text{Equation 3-1}$$

where, P is the power applied by the impeller, t the stirring time and V the volume of the emulsion template. The power (P) was calculated using equations 3-2 and 3-3:

$$P = P_o \rho_{ave} N^3 D_i^5 \quad \text{Equation 3-2}$$

where P_o is the power number, a dimensionless number depending on the geometrical details of the impeller and the reactor. P_o for the combination of reactor and anchor shaped glass stirrer used is 0.22 and was previously adopted by us for the same geometry.¹⁷⁴ The other three terms in the equation are the rotational speed of the impeller (N), the impeller diameter

(D_i) and the average emulsion density (ρ_{ave}). The average emulsion density was calculated as follows:

$$\rho_{ave} = \varphi \rho_d + (1 - \varphi) \rho_c \quad \text{Equation 3-3}$$

where ρ_c and ρ_d are the densities of the continuous and dispersed phase respectively and φ the phase volume ratio of the emulsion.

The Reynolds number (Re) describes the flow pattern inside the reactor vessel. In order to use a constant power number, fully turbulent conditions should be reached, characterised by a Re above 10000.²⁷⁵ Re was calculated for all the combinations of stirring time and speed used:

$$Re = \frac{\rho_{ave} N D_t^2}{\mu_c} \quad \text{Equation 3-4}$$

where μ_c is the viscosity of the continuous phase. In all cases it was found to be above 10000 implying fully turbulent flow and, therefore, a constant power number was assumed.²⁷⁶ The viscosity of the continuous phase can be calculated using the double-logarithmic equation of Refutas²⁷⁷ (equations 6, 7 and 8). The first step is to obtain the Viscosity Blending Number (VBN) of each component which was calculated using equation 3-5:

$$VBN = 14.534 \times \ln[\ln(v + 0.8)] + 10.975 \quad \text{Equation 3-5}$$

where v represents the kinematic viscosity of the organic phase in mm^2/s . Then to determine the VBN of the liquid mixture Equation 3-6 was used:

$$VBN_{Mixture} = \sum_{i=0}^N x_i \times VBN_i \quad \text{Equation 3-6}$$

where x_i represents the weight fraction of each component in the blend. After the VBN of the mixture was calculated, the kinematic viscosity can be determined by inverting Equation 3-5:

$$v_{mixture} = \exp \left[\exp \left(\frac{VBN_{Mixture} - 10.975}{14.534} \right) \right] - 0.8 \quad \text{Equation 3-7}$$

3.4 Characterization of macroporous polymers produced

3.4.1 Morphology of macroporous foams

Scanning electron microscopy (SEM, JCM-6000, Jeol GmbH, Eching, Germany) with an accelerating voltage of 15 kV was used to analyse fractured samples of the polymerized emulsions. The samples were fixed to a sample holder using carbon stickers and then gold coated in an argon atmosphere to guarantee the necessary conductivity (JFC-1200, JEOL GmbH, Eching, Germany). To determine pore and pore throat sizes SEM images were analysed using the imaging software ImageJ, in each image a minimum of 200 pores and pore throats was examined. The relative pore throat size was calculated using Equation 3-8, presented below:

$$d_{pt/p}[\%] = \frac{d_{pt}}{d_p} \quad \text{Equation 3-8}$$

where d_{pt} represents the average pore throat size and d_p the average pore size.

3.4.2 Density and porosity of macroporous foams

The skeletal density of crushed samples from the beads and monoliths produced was determined using helium displacement pycnometry (Micromeritics AccuPyc II 1340, Micromeritics, Neupurkersdorf, Austria). The skeletal density ρ_s is obtained as the ratio between the mass m determined using an analytical balance and the measured sample volume V .

$$\rho_s = \frac{m}{V} \quad \text{Equation 3-9}$$

Once the skeletal density is known, the foam or envelope density ρ_e and the percentage porosity were measured using an envelope density analyser (Micromeritics GeoPyc 1360, Micromeritics, Neupurkersdorf, Germany). The measurements were done using a 12.7 mm cell and piston system. The porosity of the samples (P) was calculated using the following equation:

$$P = \left(1 - \frac{\rho_e}{\rho_s}\right) \times 100 \% \quad \text{Equation 3-10}$$

where ρ_e is the foam density and ρ_s is the skeletal density.

3.4.3 Mechanical properties of macroporous monoliths

The size and shape of the macroporous beads produced from multiple emulsion templates is largely influenced by the rheological properties of the emulsion, which in turn are related to the internal phase volume ratio and surfactant concentration. Due to our inability to produce beads with comparable size and shapes, the mechanical properties of macroporous monoliths were determined instead of beads. Monoliths for compression test were prepared using sliced pieces of 50 ml centrifuge tubes as moulds. The centrifuge tubes were cut into cylinders of approximately 12 mm height and 25 mm diameter, the bottom of each piece was sealed with flexible Parafilm (Bemis Packaging, Germany) to avoid leaking of emulsion from the moulds. Six moulds per formulation were filled with emulsion and positioned in a plastic Petri dish that was carefully placed into UVC-8 Curing Conveyor System (Dymax Europe GmbH, Wiesbaden, Germany). The samples were cured using a 100 % of intensity while the conveyor belt speed was kept constant at 1.1 m/s exposing the samples to UV light approximately 1 min/run. The samples were placed in the conveyor belt a minimum of 4 times in order to form a solid layer on the surface, the same process was repeated to polymerize the bottom side of the samples. Although for emulsion droplets four runs into the UVC-8 Curing System were sufficient to obtain solid beads, it was noted that monoliths after the fourth run started to get hot. Therefore, it was decided to reduce the intensity to 90 % to prevent possible phase separation or damage of the samples due to excessive heat. After the initial irradiation, the samples were placed for 8 h under a 100 W mercury UV light (UVP Blak-Ray B100AP, Ultra-Violet Products Ltd., Cambridge, UK) to complete polymerization. The distance between the UV light and the surface of the samples in this case was 150 mm. The solidified samples were removed from the moulds and placed overnight in a sealed container immersed in a mixture of ethanol and water in order to remove all unreacted chemicals. In order to complete purification, the samples were left overnight in distilled water and after that vacuum dried at 60°C for 12 h. To obtain samples with the same dimensions, the monoliths were polished using sand paper to cylindrical pieces with a thickness of 10 mm and a diameter of 25 mm. Care was taken to ensure that both surfaces of the samples were flat and parallel. Compression tests were carried out using at least five samples of each formulation. Each test specimen was compressed at room temperature in an Instron universal tester (Model 5969, Instron GmbH, Buckinghamshire, UK) equipped with a 50 kN load cell at a compression rate of 1 mm/min until the thickness was reduced to 50 % of the original height. The compression plates were

sprayed with a dry TEFLON (PTFE) spray (Ballistol, Klever GmbH, Germany) to minimize friction and barrelling between the compression plates and sample. The Young's modulus was calculated from the slope of the initial linear elastic region of the stress/strain curve. Crush strength was obtained using the maximum compressive strength of the sample at the end of the linear elastic region. The measured compression data was analysed using the software Origin Pro 9.0G.

3.4.4 Thermal stability of polymer foams

The thermal stability of the materials produced was investigated using thermogravimetric analysis (TGA). TGA measures the mass change of a sample as a function of temperature, which was increased at a constant heating rate in nitrogen atmosphere (flow rate of 25 cm³/min) to avoid an oxidative decomposition. All thermogravimetric measurements were conducted using a Discovery TGA (TA Instruments, Eschborn, Germany) in a temperature range from 30°C to 550°C. First the samples were heated from 30°C to 120°C at a heating rate of 10°C/min and then the temperature was held for 15 min in order to remove any residual moisture present in the sample. After the plateau, the temperature was increased at 10°C/min until 550°C were reached. The sample size used was 10 to 20 mg. The samples were weighted before on a platinum pan. Through analysis of the data, conclusions over the thermal stability were obtained, namely the initial decomposition temperature which provides a measure of the thermal stability of the material. The decomposition temperature (T_x) is defined as the temperature at which 10 % of the material degraded. The degradation temperature (T_y) was obtained, which was defined as the temperature at a weight loss of 50 %.

3.4.5 Size distribution of macroporous beads

To perform particle size analysis a Helos KR (Sympatec GmbH, Germany) laser diffraction sensor equipped with a wet dispersion system was used. The measurements were performed using a 50 ml cuvette filled with ethanol and equipped with a software controlled magnetic stirrer coated with PTFE. After calibration, the samples were added into the cuvette until an optical concentration (C_{opt}) of approximately 15 % was achieved. A common alternative to represent the particle size distribution is the use of the average bead size along with one or more values to describe the size dispersion. In this thesis, following common practice in the

literature, the average bead size and the coefficient of variation (CV) calculated as the ratio between the standard deviation σ and the mean bead size μ as presented below were used:

$$CV = \frac{\mu}{\sigma} \quad \text{Equation 3-11}$$

3.4.6 Yield of macroporous beads produced in a plug flow reactor

Emulsion templates were injected into the a recirculating carrier phase (W_2) using a syringe pump (Ultimus IV, Nordson EFD, Pforzheim, Germany) that allows to accurately dispense emulsion volumes as small as 0.1 μL . In order to determine the total volume of emulsion transformed into porous beads, the total volume of beads produced was determined using an envelope density analyser (GeoPyc 1360, Micrometrics Ltd., UK). The yield of the process was calculated as follows:

$$\text{Yield [\%]} = \frac{\text{Beads obtained [cm}^3\text{]}}{\text{Emulsion injected [cm}^3\text{]}} \times 100 \% \quad \text{Equation 3-12}$$

Chapter 4. Effect of emulsion template composition on pore structure of macroporous beads produced by sedimentation polymerisation

4.1 Introduction

The monomer methyl methacrylate (MMA) together with ethylene glycol dimethylacrylate (EGDMA) as crosslinker were used as organic continuous phase. The dispersed phase of the emulsion consisted in a calcium chloride ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$) electrolyte. The emulsion was stabilised using the non-ionic surfactant poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol, commercially available as Pluronic L-81. The production process of macroporous beads from photopolymerisable emulsion templates requires a few minutes to a few hours depending of the amount of beads needed and the synthesis conditions. For that reason, another objective was to investigate the emulsion stability over time, in order to evaluate their compatibility with the production times required to synthesise beads. Additionally, the rheological properties of the emulsions were examined. With this information, the ability of each formulation to create spherical porous polymer beads with open or closed pore morphology was identified. Furthermore, compression tests were performed on monoliths obtained from each emulsion template formulation.

4.1.1 Relation between bead shape and rheological behaviour of the emulsion templates

Macroporous spherical beads are desirable for certain applications, such as column materials for chromatography applications.¹⁹⁴ Moreover, the possibility to synthesise macroporous particles with non-spherical shapes greatly increases the application range. Beads with a variety of shapes can be produced using sacrificial templates²⁷⁸ or special channel setups.²⁷⁹ A simple method to obtain non-spherical beads is the use of polymerisable highly viscous emulsions. In this case, the shape of beads will be defined by the shape of the emulsion droplet at the gel point. The use of emulsion templates stabilised by different surfactant concentrations and internal phase volume ratios influences not only the morphology of the porous polymer foams produced but can also be used to tailor the rheological properties of the emulsion templates. This pathway to obtain non-spherical beads was studied by Gokmen et al.^{199,202} using highly viscous W_1/O HIPEs that after injection into a secondary aqueous phase

(W₂) formed elongated droplets or rods that preserved the shape during polymerisation. PEO-PPO-PEO surfactants with different molar weights were used to stabilise methacrylate based W₁/O HIPEs, leading to emulsion templates with different viscosities. The emulsion templates were injected into a tubing based microfluidic device and depending on the viscosity of the HIPEs, spherical or elongated droplets formed after injection into a secondary aqueous phase (W₂). In their work, the surfactant poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) with the trade name Pluronic L-81 proved effective to stabilise HIPEs with rather low viscosities. Pluronic L-81, also called in the literature PEG-PPG-PEG (E3P43E3), is a block copolymer consisting of 43 poly(propylene oxide) groups in the centre and 3 poly(ethylene oxide) groups at its respective ends.²⁸⁰ According to the manufacturer (BASF Österreich GmbH, Vienna, Austria), this surfactant has a molecular weight of 2800 g/mol and a HLB of 2.0. To determine which formulations can be used to produce spherical beads with a controlled size and size dispersion, it is necessary to understand the behaviour of the emulsion templates when they are injected into a secondary aqueous phase (W₂). Therefore, emulsion templates with different concentrations of this surfactant and internal phase volume ratios were produced and their ability to form spherical droplets and later beads after polymerisation studied.

4.1.2 Mechanical properties of macroporous monoliths

A better understanding of the mechanical properties of the polymeric foams is essential if the aim is to tailor the release conditions of an encapsulated active ingredient to the environment. Porous polymer beads tailored to release an encapsulated active ingredient under specific conditions, such as fracture under a predetermined load, progressive erosion or after degradation of a protective superficial layer are especially attractive for the Oil & Gas industry. Additionally, porous polymer beads that are able to keep their structural integrity while at the same time deliver the encapsulated substance can be separated, recovered and reused if necessary when the process is completed. It is well known that the mechanical properties of porous materials produced by emulsion templating can be modified by controlling the foam density, energy input during emulsification^{21, 174} and by choosing a suitable combination of monomer and crosslinker.²⁸¹ Flexible porous polymers can be synthesised using emulsion templating as well as materials with varying stiffness.²⁸² Brittleness and friability can be controlled by varying the amount of surfactant used to stabilise the emulsion template.⁵⁸ In

order to obtain mechanically strong porous polymers, MMA as monomer and EGDMA as crosslinker were chosen as they have been successfully used before to create porous polymers with excellent mechanical properties.²¹

The main objective of the work presented in this chapter was to identify the transition zones from closed to open porous structures in macroporous beads by controlling the internal phase volume ratio (ϕ) and the surfactant concentration used to stabilise the emulsion templates.

4.2 Experimental

4.2.1 Synthesis of macroporous beads via “sedimentation polymerisation”

In order to create macroporous beads, a 5 ml syringe was filled with approximately 4 mL of emulsion and equipped with a straight 22 gauge needle (I.D. 0.41 mm) at the end. The tip of the needle was submerged into a 10 cm diameter Petri dish containing the same aqueous solution as used as internal phase of the emulsion template. Using a syringe pump (Ultimus IV, NordsonEFD, Pforzheim, Germany) controlled amounts of emulsion were dispensed into the aqueous solution creating between 20 and 30 droplets of approximately 2 mm. The shape and size of the droplets produced was determined by the formulation used and the amount of emulsion injected. After injection, the Petri dish containing the emulsion droplets was exposed to UV-light (UVC-8 Curing Conveyor System, Dymax Europe GmbH, Wiesbaden, Germany). This machine was equipped with a 2000 W mercury bulb 180 mm above the surface of the conveyor belt and it was used at 100 % intensity. According to the manufacturer, the maximum intensity of the curing system is 800 mW/cm² with an irradiation peak at 365 nm (Figure 4-1) for a new bulb working at 60 mm distance from the conveyor belt. The conveyor belt speed was kept constant at 1.1 m/s giving an approximate exposure time of 1 min/run, each Petri dish was placed onto the conveyor belt a minimum of 4 times. In order to complete polymerization the Petri dish with the solidified droplets was placed under a 100 W mercury UV light (UVP Blak-Ray B100AP, Ultra-Violet Products Ltd., Cambridge, UK) at a distance of 100 mm.

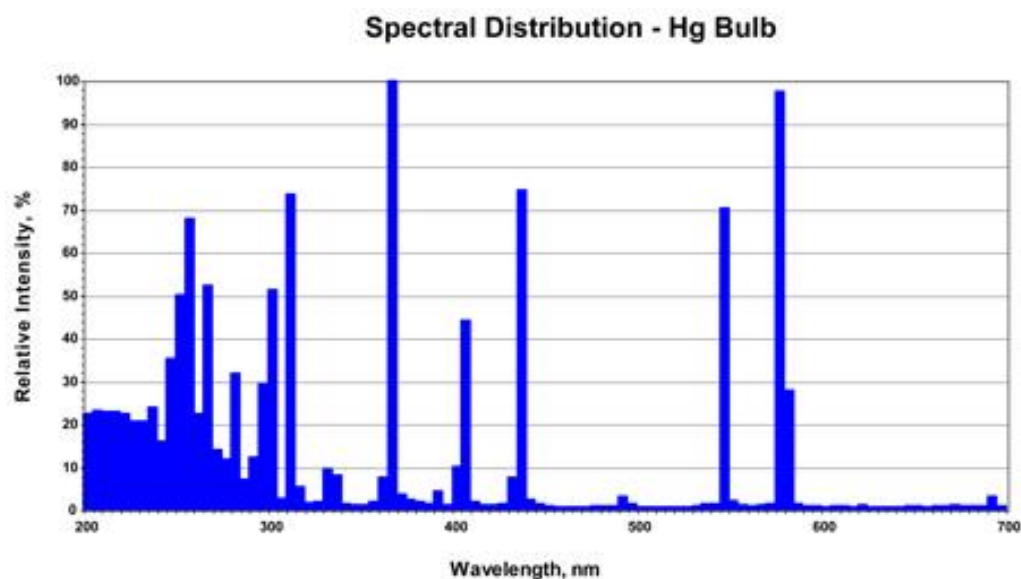


Figure 4-1. Spectral distribution of the UVC-8 Curing Conveyor System used.²⁸³

The reaction was terminated by switching off the UV source after 30 min. The solidified droplets were removed from the Petri dish and placed overnight in a sealed container immersed in a mixture of ethanol and water to extract any unreacted chemicals. To completely purify the samples, they were washed and left overnight in distilled water and after that vacuum dried at 60°C for 12h

Summary of the formulations used

A summary of all formulations used can be found in Table 4-1. The coding of emulsions is as follows. The letter E stands for emulsion formulation, while the surfactant concentration used to stabilise the emulsion template (vol.% with respect to the organic phase) is indicated with the first numeric digits of the emulsion code. The last two digits of the emulsion formulation code represent the internal phase volume ratio. As an example, the emulsion E15-70, was stabilised using a surfactant concentration of 15 vol.% and had an internal phase volume ratio of 70 %.

Table 4-1. Summary of the nomenclature and emulsion template formulations used.

Formulation	Surfactant concentration in M/HIPE ^a [%]	Internal phase volume ratio [%]	Volume of initiator used ^b [cm ³]
E5-50	5	50	0.35
E5-60	5	60	0.35
E5-70	5	70	0.3
E5-80	5	80	0.25
E5-90	5	90	0.25
E10-50	10	50	0.35
E10-60	10	60	0.35
E10-70	10	70	0.3
E10-80	10	80	0.25
E10-90	10	90	0.25
E15-50	15	50	0.35
E15-60	15	60	0.35
E15-70	15	70	0.3
E15-80	15	80	0.25
E15-90	15	90	0.25
E20-50	20	50	0.35
E20-60	20	60	0.35
E20-70	20	70	0.3
E20-80	20	80	0.25
E20-90	20	90	0.25
E25-50	25	50	0.35
E25-60	25	60	0.35
E25-70	25	70	0.25
E25-80	25	80	0.25
E25-90	25	90	0.25
E30-50	30	50	0.35
E30-60	30	60	0.3
E30-70	30	70	0.25
E30-80	30	80	0.25
E30-90	30	90	0.25
^a Surfactant concentrations are with respect to monomer phase			
^b Photoinitiator used in the organic phase			

4.3 Results and discussion

4.3.1 Stability of emulsion templates

The production of macroporous polymer beads from emulsion templates is strongly influenced by the stability of the primary W_1/O emulsion template over time. The W_1/O emulsion should be stable during the entire bead production process, namely, filling the syringe with the primary emulsion and the injection into the secondary aqueous emulsion phase (W_2) until the emulsion droplets are fully polymerised. Typically, the minimum amount of time needed to create beads after emulsification was completed varied between two and 30 min. In order to evaluate the suitability of the different emulsion formulations for the

production of macroporous beads, emulsion templates were produced and their stability was visually assessed at regular intervals. To evaluate the stability of the emulsion templates, when the first signs of destabilisation, such as sedimentation or coalescence, were observed, that point was considered as the starting point of phase separation. An example of this can be seen in Figure 4-2, which shows emulsions with an internal phase volume ratio of 60 % stabilised by different amounts of surfactant. For that amount of dispersed phase, increasing the surfactant concentration from 15 to 25 vol.% resulted in a major increase of the emulsion stability from several minutes to weeks. On the contrary it was impossible to prepare stable emulsions with surfactant concentrations below 5 vol.%, while for emulsions stabilised with 10 vol.% signs of destabilisation were visible after a few minutes.



Figure 4-2. Photographs of emulsions with an internal phase volume ratio of 60 % stabilised by different surfactant concentrations. From left to right, the first three emulsions were stabilised by 5, 10 and 15 vol.% of surfactant and phase separated after a few minutes. The last three were stabilised using 20, 25 and 30 vol.% of surfactant. No signs of phase separation were visible after one week.

Emulsion prepared with internal phase volume ratios between 50 and 70% and surfactant concentrations below 5 vol.% resulted in unstable emulsions that destabilised a few seconds after emulsification. The starting point of destabilisation of all the emulsions prepared is presented in Figure 4-3. It can be observed that more stable emulsions were produced when higher surfactant concentrations were used. In the case of emulsions with an internal phase volume ratio of 50 % (MIPeS), surfactant volumes above 15 vol.% were needed to obtain emulsions that were stable for more than 10 min. Emulsions prepared with an of internal

phase volume ratio above 60 % and surfactant concentration higher than 15 vol.% were stable for periods over 30 min without any visible signs of destabilisation.

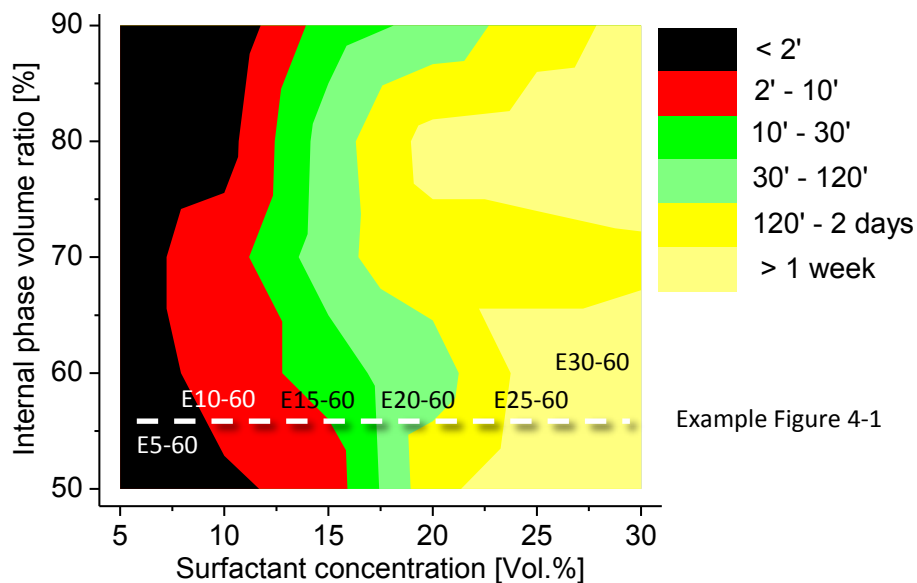


Figure 4-3. Onset of phase separation in emulsions with different internal phase volume ratios stabilised with increasing surfactant concentrations. The stability of emulsions with an internal phase volume ratio of 60 % shown in Figure 4-2 is presented.

When ϕ was increased to 90 vol.% and the emulsion stabilised using surfactant concentrations below 5 %, phase separation occurred almost instantly after emulsification. For emulsions stabilised with a surfactant concentration between 5 vol.% and 10 vol.%, any attempt to re-emulsify the aqueous phase by manually shaking the centrifuge tube led to phase inversion. In this case, phase inversion was verified by injecting emulsion in two glass vessels containing the electrolyte used as internal phase and a small amount of continuous phase. Droplets formed after the emulsion was injected in the glass vessel filled with continuous phase. When emulsion was injected in the aqueous solution, it dispersed immediately without forming droplets. A homogenous emulsion with an internal phase volume ratio of 90 % was obtained when the surfactant concentration was increased to 15 vol.%. However, after approximately 10 min a small amount of water became visible at the bottom of the centrifuge tube indicating the onset of phase separation.

4.3.2 Rheological behaviour of emulsions with increasing surfactant concentration and internal phase volume ratio

The absolute viscosity of a primary W_1/O emulsion at a specific shear rate is not enough to predict whether it can be injected through a needle into a secondary aqueous phase to form monodisperse $W_1/O/W_2$ spherical emulsion droplets. In order to describe the rheological behaviour or apparent viscosity of each formulation in a simple way and compare the different formulations tested, the emulsions were classified as shown in Table 4-2. Formulations with a viscosity similar to milk or cream formed spherical droplets after injection of the primary emulsion into the secondary aqueous phase (W_2), leading to spherical beads after polymerisation. When formulations with a viscosity similar to mayonnaise were used, elongated droplets with a diameter similar to the inner diameter of the needle formed. Once polymerised, the non-spherical droplets resulted in rod-like structures. The use of viscous HIPEs to obtain non-spherical polyHIPEs segments was already reported by Du Prez et al.²⁰² They used a primary emulsion stabilised with a high molecular weight (MW) surfactant (PEO-PPO-PEO MW 4400 g/mol) that after injection into a microfluidic device formed emulsion segments due to the jetting effect. After downstream photopolymerisation, the segments became solid “rods”.

Table 4-2. Classification of emulsion rheological behaviour

Similar rheological behaviour or Psychorheology	Flow behavior
Water	Fast and continuous
Milk	Fast and continuous
Milk cream	Regular and continuous
Liquid honig	Slow and continuous
Mayonnaise	Slow and intermitent (chunks)
Cottage cheese	No flow was observed

The flow behaviour of the emulsions was influenced by two main drivers, the surfactant concentration used to stabilise the emulsion and the internal phase volume ratio. The viscosity of the continuous oil phase used was determined by the viscosity of the monomers used in the formulation (MMA $\eta = 0.53$ mPa·s and EGDMA $\eta = 3.20$ mPa·s according to the manufacturer) and the surfactant concentration (Pluronic L-81 $\eta = 475$ mPa·s)²⁸⁰ used to stabilise the emulsion. Higher amounts of surfactant led to an increase in the viscosity of the

organic phase, which became similar to cooking oil and increased the apparent viscosity of the emulsion with low internal phase ratios (Figure 4-4).

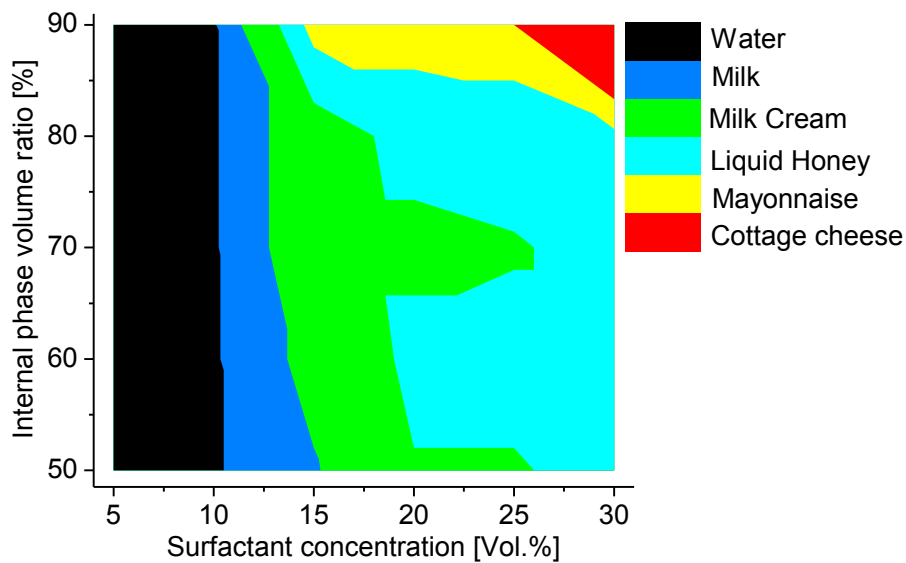


Figure 4-4. Rheological behaviour of emulsions with different internal phase volume ratios stabilised with increasing amounts of surfactant.

The apparent viscosity of the emulsions also increased dramatically when the amount of dispersed phase exceeded 70 %. This percentage is close to the theoretical maximum dense packing configuration for equal sized droplets (74.05 %), which defines high internal phase emulsions (HIPEs).⁴⁵ The addition of more dispersed phase will cause the deformation of the spherical droplets in the contact points with the neighbouring droplets restricting movement and increasing viscosity.^{45, 48} The same increase in viscosity is expected in systems with a broad droplet size distribution,¹⁵⁸ such as the ones studied in this work. For emulsions with a rheological behaviour similar to milk or cream, spherical emulsion droplets formed when the W_1/O emulsion was injected into W_2 since interfacial tension aims to minimise the contact area between the two phases. In the case of emulsions with higher viscosities, similar to liquid honey, elongated droplets were formed after injection into W_2 and in most cases the W_1/O emulsion droplets became spherical after a few seconds. Emulsions with a rheological behaviour similar to liquid honey appear to be in a transition range between spherical and elongated droplets. In this case, the interfacial tension forces and the resistance of the droplets to change their shape because of the higher viscosities were similar. This effect, combined with the rapid solidification due to photopolymerisation of the non-spherical emulsion droplets before they formed a spherical shape allowed us to produce elongated

beads or rods. This behaviour was used for the production of macroporous non-spherical beads and filaments from multiple emulsion templates using a co-flow setup, which is described in Chapter 6. When emulsions with a viscosity similar to mayonnaise or cottage cheese were injected into the secondary aqueous phase (W_2) threads of emulsion of different lengths formed. In both cases it was necessary to manually cut the emulsion thread as it did not detach from the needle tip used for injection.

4.3.3 Internal morphology of the macroporous beads produced

We found that the stability of the emulsions injected had a significant impact on the final morphology of the beads produced. When formulations E5-80, E5-90 and E10-90 were used it was not possible to create stable W_1/O emulsions. After the stirring was complete, droplets of the emulsion started to coalesce leading to an almost complete phase separation in a few seconds after stirring was finished (Figure 4-5).

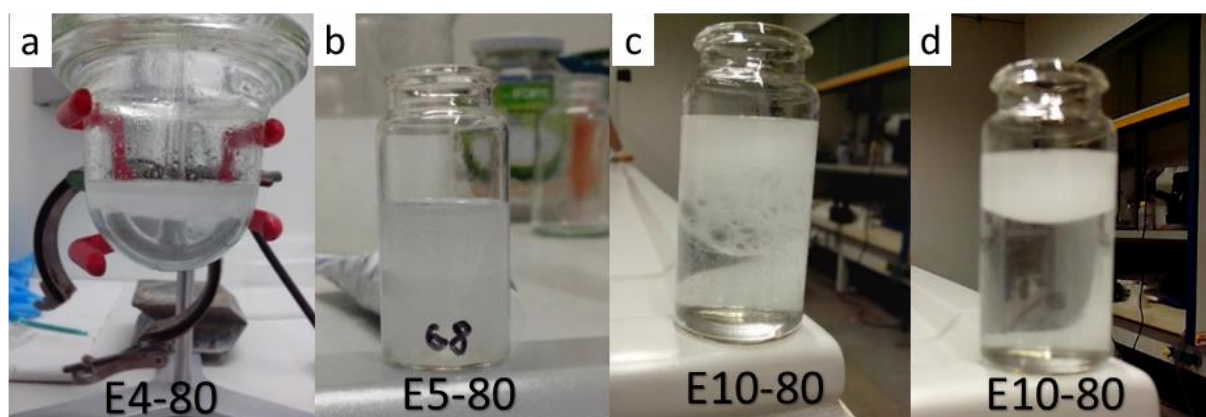


Figure 4-5. Photographs of emulsions with an internal phase volume ratio of 80 % stabilised with a surfactant concentration of 10 vol.% or less having different degrees of destabilisation. a) Emulsion stabilised with 4 vol.% of surfactant 1 min after stirring is finished b) Emulsion E5-80, 1 min after stirring, sedimentation is already visible c) and d) Emulsion E10-80 10 min and 15 min after stirring, showing phase separation.

The internal pore morphology of all beads produced is shown in Figure 4-6. W_1/O emulsions containing an internal phase volume ratio between 50 % and 70 % stabilised with a surfactant concentration of 5 vol.% produced beads with only a few large pores after polymerisation. This can be explained by the destabilisation of the emulsion templates. When the surfactant concentration used was insufficient to effectively stabilise the emulsion templates, droplet

coalescence led to the formation of almost non-porous beads after polymerisation. Emulsions stabilised by surfactant concentrations of 10 vol.% or less were stable only for a short amount of time, the beads produced after polymerisation had large pores and a broad pore size distribution. Partial destabilisation was also present in formulations stabilised with a surfactant concentration of 10 vol.% and 15 vol.%. The emulsions E10-50, E10-60, E10-70, E10-80 and E15-50 after polymerisation resulted in beads with large non-interconnected pores, which were the product of early coalescence of the emulsion prior to polymerisation. This effect is evidenced by the broad pore size distribution of beads produced from these emulsion templates, where the average standard deviation of pore size was between 1 and 3 times larger than the average pore size (Figure 4-6). The beads produced by polymerisation of M/HIPES stabilised by a surfactant concentration of 15 vol.% and different internal phase volume ratios had a more homogeneous pore size distribution, indicating that the emulsion template was more stable. In this case, the pore size dispersion was similar to the average pore size (Table A4-1 in the supporting information).

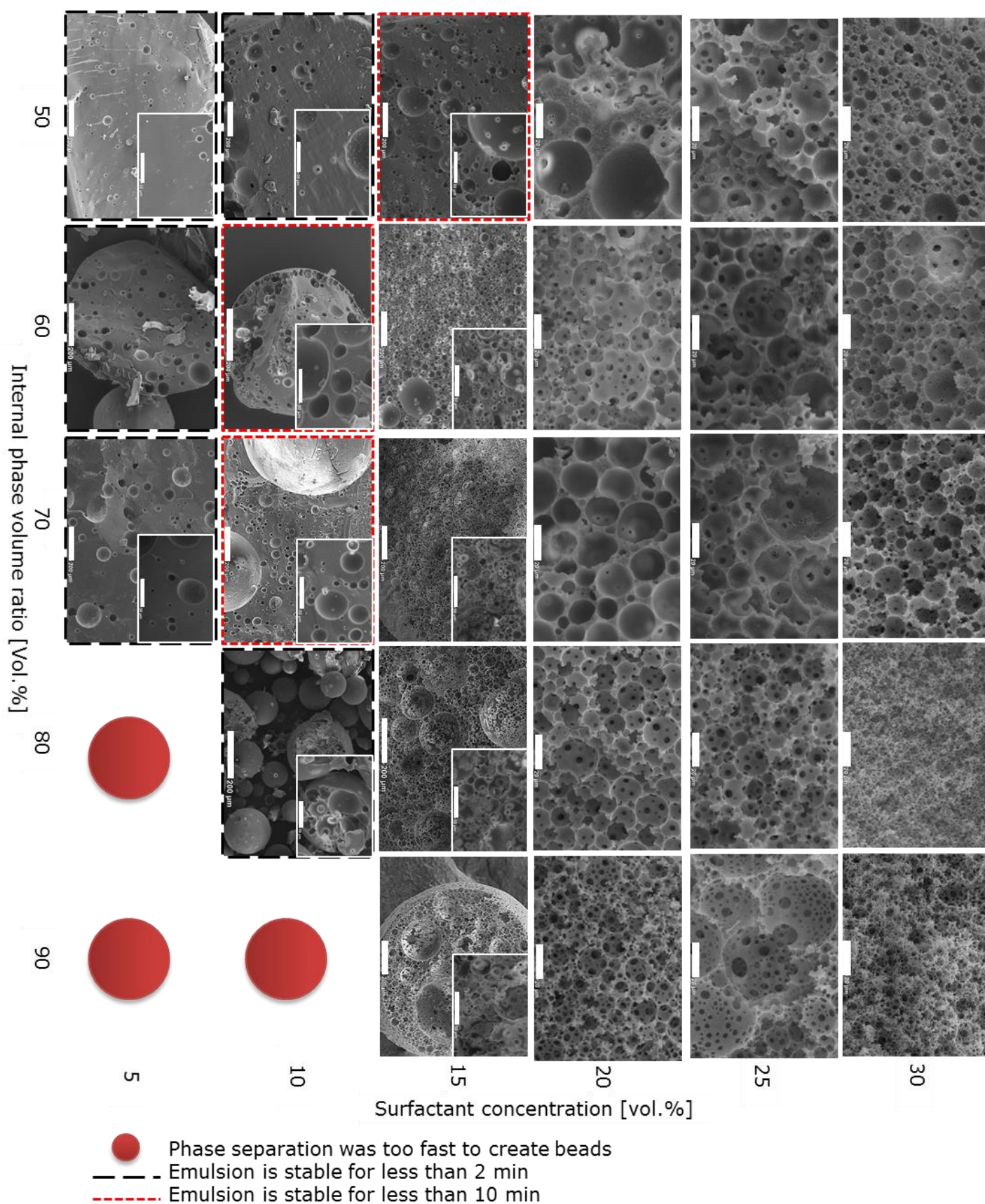


Figure 4-6. SEM images of the internal pore morphology of the beads produced by sedimentation polymerisation. Scale bars in images of beads from emulsions stabilised with: 20 vol.% surfactant concentration or more are 20 μm , in images of beads from emulsion templates stabilised with 15 vol.% or less surfactant concentration the scale bar is 200 μm . The scale bars in inserts are 50 μm .

Influence of surfactant concentration in the emulsion templates on pore size of beads

In general, it was observed that the average pore size of beads decreased when increasing surfactant concentrations were used to stabilise the emulsion templates (Figure 4-7). This becomes more evident in beads produced by polymerisation of emulsion templates stabilised with a surfactant concentration above 15 vol.%. In this case, beads with a narrow pore size distribution were obtained, as indicated by the lower pore size standard deviation (Table A2-1 in the Annex 1 support information). In the case of beads obtained by polymerisation of emulsion templates stabilised with surfactant concentrations lower than 15 vol.%, an internal pore structure with broad pore size distribution was obtained in almost every sample. This was indicated by the average pore size standard deviation, which was higher than the average pore size, indicating a poor stability of the emulsion templates. The evidence suggested that a threshold has been reached where the influence of the surfactant concentration on the emulsion stability seems sufficient to significantly reduce droplet coalescence in the emulsion templates. Emulsions stabilised with a surfactant concentration of 30 vol.% produced porous beads with an even narrower pore size distribution for every internal phase volume ratio used. In this case, the standard deviation in pore size for all samples was between 30 and 45 % of the average pore size.

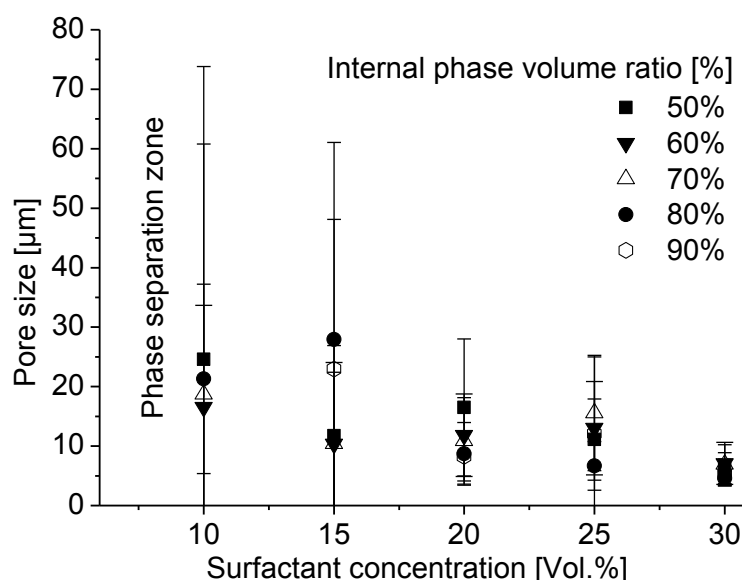


Figure 4-7. Average pore size of beads produced by polymerisation of emulsion templates with different internal phase volume ratios stabilised with increasing surfactant concentrations

Influence of surfactant concentration in the emulsion templates on beads pore throat size

The surfactant concentration used to stabilise the emulsion templates had a significant effect on the pore interconnectivity of the beads formed after polymerisation. Beads produced from emulsions stabilised using lower amounts of surfactant tend to have larger pore throats (Figure 4-8).

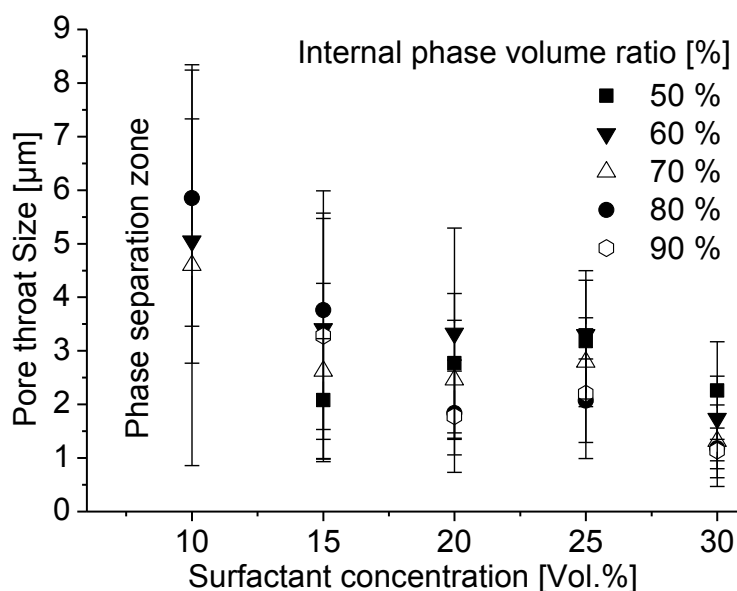


Figure 4-8. Pore throat size of beads obtained from emulsion templates with different internal phase volume ratios and stabilised with increasing surfactant concentrations. Emulsions stabilised with increasing concentration of surfactant led to a reduction in pore throat size.

It was observed that polyHIPEs produced from emulsion templates with a broader droplet size distribution contained more efficiently packed pores.¹⁷¹ This effect increases contact between droplets and droplet deformation,¹⁷⁴ which promotes the formation of thin films that are believed to be the origin of pore throat formation during polymerisation. Emulsion templates with a broad droplet size distribution can be result of a low energy input during emulsification or coalescence of internal phase droplets due to poor stability. The narrow pore size distribution observed in beads produced by polymerisation of emulsion templates emulsified with a similar energy input, but stabilised with higher surfactant concentrations, suggests a limited stability of the emulsion templates. Beads synthesised from emulsions with limited stability, for example, emulsions stabilised with surfactant concentrations of 5 vol.%, did not have interconnecting pore throats. When the surfactant concentration in the emulsion templates was increased to 10 vol.%, only a few large pore throats were observed providing

interconnectivity to the internal structure of the beads (Table A4-2 in the supplementary information). Emulsion templates stabilised with higher surfactant concentrations produced beads with a larger number of smaller pore throats after polymerisation, contributing to a more interconnected or open pore structure.

Influence of internal phase volume ratio of the emulsion templates on pore and pore throat size of beads

Increasing the internal phase volume ratio of the emulsion templates did not significantly influence the average pore size (Figure A4-1 in the support information). However, a trend to smaller pore throats was noted in beads prepared by polymerisation of emulsion templates with increasing internal phase volume ratios. This trend was observed in all samples with the exception of beads produced from emulsion templates stabilised with surfactant concentrations below 15 vol.% (Table 4-3).

Table 4-3. Pore throat size of beads obtained from emulsion templates with different internal phase volume ratios and stabilised with increasing surfactant concentrations.

		Pore throat size [μm]				
Surfactant concentration [vol.%]	30	2.3 ± 0.9	1.7 ± 0.8	1.3 ± 0.7	1.2 ± 0.4	1.1 ± 0.7
	25	3.2 ± 1.1	3.3 ± 1.2	2.8 ± 0.8	2.1 ± 0.8	2.2 ± 1.2
	20	2.8 ± 1.3	3.3 ± 2.0	2.5 ± 1.1	1.8 ± 0.8	1.8 ± 1.1
	15	2.1 ± 1.2	3.4 ± 2.1	2.6 ± 1.6	3.7 ± 2.2	3.3 ± 2.3
	10	Non - interconnected pores No emulsion formed				
	5					
		50	60	70	80	90
		Internal phase volume ratio [%]				

After calculation of the relative pore throat size (Equation 3-8), a relation between the average pore size and the average pore throats size with increasing surfactant concentration cannot be clearly identified (Table 4-4). However, it was observed that the number of pore throats in each pore increased with increasing surfactant concentrations used to stabilise the emulsion templates for every internal phase volume ratio used.

Table 4-4. Relative pore throat size of beads produced by polymerisation of emulsion templates with different internal phase volume ratios and surfactant concentrations. The use of surfactant concentrations below 5 vol.% led to the formation of beads with closed pores.

		Relative pore throat size [%]				
Surfactant concentration [vol.%]	30	37 ± 32	24 ± 23	19 ± 12	26 ± 33	20 ± 32
	25	29 ± 16	25 ± 15	18 ± 12	31 ± 19	18 ± 9
	20	17 ± 11	28 ± 29	23 ± 15	21 ± 15	22 ± 26
	15	18 ± 8	33 ± 15	25 ± 13	14 ± 7	14 ± 9
	10	Non - interconnected pores		31 ± 13	25 ± 7	28 ± 15
	5			No emulsion formed		
		50	60	70	80	90
		Internal phase volume ratio [%]				

4.3.4 Compression properties of macroporous polymer monoliths produced by polymerisation of emulsion templates with different surfactant concentrations and internal phase volume ratios

The surfactant concentration and internal phase volume ratio used to produce emulsion templates have a critical influence on the mechanical properties of the macroporous polymers produced.¹⁷⁵ A better understanding of the relations between the emulsion template composition and mechanical properties of the polymeric materials produced after polymerisation is essential to control the release conditions of beads used as delivery systems. Compression tests are commonly used for the characterisation of porous polymer materials. However, due the different rheological properties of the emulsions used, it was not possible to produce beads with identical size and shape. Therefore, the mechanical properties of macroporous monoliths were determined. Compression tests were performed on UV polymerised monoliths obtained from each emulsion template previously used to understand the influence of those parameters in the mechanical properties.

During sample preparation, it was noted that after pouring the emulsion templates into the moulds used to produce monoliths, the emulsions were less stable than emulsion templates previously observed in section 4.3.1 (Figure 4-2). The reduced emulsion stability due to the longer polymerisation times required to produce monoliths compared with the polymerisation times required to produce beads limited the emulsions suitable to produce monoliths after polymerisation. No monoliths for compression test could be prepared by UV

photopolymerisation of emulsions templates stabilised using a surfactant concentration of 5 vol.% or less due to early phase separation. Then, emulsion templates with increasing internal phase volume ratios were prepared using a surfactant concentration of 10 vol.% but samples for compression testing could only be produced using the formulation E10-60. In all the other samples prepared containing an internal phase volume ratio of 60 % dramatic phase separation occurred due to the poor stability of the emulsion. Monoliths prepared after polymerisation of emulsion templates E10-60 were hard and contained a few pores on the surface with an approximate diameter of 2 mm. The large pores obtained seem to indicate an early destabilisation of the emulsion templates during polymerisation (Figure 4-9). Macroporous polymers produced by polymerisation of the emulsion template E10-60, had a porosity of $71 \pm 2 \%$, a Young's Modulus of 125.8 ± 13.3 MPa and a crush strength of 5 ± 0.5 MPa.



Figure 4-9. Compression test samples synthesised from emulsion templates E10-60. The internal pore structure contained a few large pores with a size between 3-6 mm.

Emulsion templates with internal phase volume ratios from 50 to 90 % and stabilised with a surfactant concentration of 15 vol.% produced suitable samples for compression testing after polymerisation, except for the formulation E15-70, which underwent phase separation before polymerisation was possible. As expected due to their higher density, monoliths produced from emulsion templates with a low internal phase volume ratio (E15-50 and E15-60) possessed the highest Young's modulus of all formulations tested so far, 186.5 ± 10.6 MPa and 137.6 ± 10.6 MPa, respectively. The crush strength of monoliths produced using formulation E15-50 was 8.4 ± 0.3 MPa. In the case of monoliths produced using formulation E15-60, the crush strength was 8.3 ± 0.3 MPa. Monoliths produced using formulating E15-50 had a porosity of $56 \pm 2 \%$, while monoliths produced by polymerisation of emulsion templates E15-60 had a porosity $71 \pm 2 \%$. In the case monoliths produced by polymerisation of emulsion templates containing an internal phase volume ratio of 80 and 90 %, all the samples produced

after polymerisation were friable. Therefore, special care had to be taken when removing the samples from the moulds to avoid fractures. Increasing the surfactant concentration in the emulsion templates to 20 vol.% resulted in a visible change on the monoliths surface after polymerisation. All the samples produced had a smooth surface with no pores visible to the naked eye (Figure 4-10). This is related not only to a reduction in pore size but more importantly a massive decrease in pore size dispersion (Figure 4-7). While samples produced from emulsion E20-50 were rather compact and difficult to break manually, increasing the internal phase volume ratio above 50 % constantly reduced the friability of the samples produced. Occasionally, demoulding the monoliths from the containers caused small fractures and detachment of small parts of the samples (Figure 4-9S2). In all cases defective samples were discarded.



Figure 4-10. Photographs of polyMIPE samples for compression test produced by polymerisation of emulsion templates E20-60. A smooth surface was visible after polishing. The sample S2 was discarded because of surface defects.

When emulsion E20-90 was used as template, only a superficial polymerisation of approximately 2 mm was achieved after the samples were exposed to UV light four times on each side completing approximately 8 min of exposure. The cure depth during photopolymerisation is influenced by various parameters, such as temperature, photoinitiator concentration, characteristics of the monomers used, irradiation time and intensity.²⁸⁴⁻²⁸⁵ The UV penetrating into the emulsion will be absorbed by the photoinitiator. However, penetration is reduced by emulsion adsorption, which is related to emulsion composition. Moreover, each system has an optimal concentration of photoinitiator for which the cure depth is maximised.²⁸⁵ Merrigan and Desmarais²⁸⁶ while working for Procter & Gamble patented a process for the production of tick porous layers (up to 10 mm) using photopolymerised HIPEs. They tested emulsion templates with different amounts of

photoinitiator dissolved in the organic phase. Complete polymerisation of the samples was achieved by placing the samples on reflective surface, allowing a uniform UV light irradiation on the surface. Lower concentrations of photoinitiator decreased the UV light absorption of the emulsion and allowed for deeper penetration of UV light into the HIPE, resulting in a higher polymerisation depth. The presence of oxygen can severely affect the radical-induced polymerisation by scavenging the radicals formed.²⁸⁷ In order to successfully polymerise a sample in an oxygen containing environment there should be enough photoinitiator to overcome oxygen inhibition.²⁸⁸ Besides photoinitiator concentration, the droplet size also plays an important role in the polymerisation of thick emulsion layers, larger aqueous droplets will reduce light scattering allowing a deeper UV light penetration.²⁸⁹ Higher surfactant concentrations used to stabilise the emulsion templates reduced the interfacial tension which promoted droplet break up during emulsification, therefore, facilitating the formation of smaller droplets. This is the reason why the use of higher surfactant concentrations reduced the cure depth in the samples (Table 4-5). In order to increase the polymerisation depth of HIPEs containing methacrylates as organic phase, a simple but effective tool is to increase the amount of energy radiated to the surface. Kimmins et al.²⁹⁰ polymerised methacrylate based HIPEs containing a blend of diphenyl (2,4,6-trimethylbenzoyl)phosphine oxide and 2-hydroxy-2-methylpropiophenone as photoinitiator (10 % v/v of monomer phase) with a thickness of 35 mm after being exposed to UV light with an intensity of 200 W/cm². While the wavelength of our UV-system was similar to the one used in their work with a peak of the relative intensity around 365 nm (Figure 4-1), the light intensity according to the manufacturer is only 800 mW/cm² at full power. Furthermore, lower concentrations of photoinitiator (2-hydroxy-2-methyl-1-phenyl-propan-1-one) were used in all our emulsions i.e. between 2 and 2.4 % v/v of monomer phase. In an attempt to polymerise the entire monolith, the samples were exposed to UV light another six times on each side achieving a total irradiation time of almost 20 min. After irradiation, the polymerisation depth was between 2 and 4 mm. A summary of the maximum polymerisation depth for a given UV light irradiation time and the visual appearance of the monoliths after polymerisation produced is given in Table 4-5. Partial polymerisation of the monoliths was observed in several samples, especially when surfactant concentrations above 25 vol.% were used to stabilise the emulsion templates.

Table 4-5. Summary of the maximum polymerisation depth for a given UV light irradiation and visual appearance of monoliths produced after polymerisation.

Emulsion formulation	Monolithic samples	Polymerization depth [mm]	UV Irradiation time [min]	Visual appearance of monoliths produced after UV irradiation
E5-50	No	Phase separation	N/A	N/A
E5-60	No	Phase separation	N/A	N/A
E5-70	No	Phase separation	N/A	N/A
E5-80	No	Phase separation	N/A	No emulsion formed
E5-90	No	Phase separation	N/A	No emulsion formed
E10-50	No	Phase separation	N/A	N/A
E10-60	Yes	> 10	6	hard - small pores visible
E10-70	No	Phase separation	N/A	N/A
E10-80	No	Phase separation	N/A	N/A
E10-90	No	Phase separation	N/A	No emulsion formed
E15-50	Yes	> 10	6	hard and brittle
E15-60	Yes	> 10	6	not friable - hard - rough surface
E15-70	Yes	> 10	4	hard - smooth
E15-80	Yes	> 10	4	brittle - small pores are visible
E15-90	Yes	> 10	4	friable - smooth
E20-50	Yes	> 10	4	smooth and hard
E20-60	Yes	> 10	6	friable - smooth and hard
E20-70	Yes	> 10	4	friable - smooth
E20-80	Yes	> 10	6	friable - smooth and hard
E20-90	Yes	2	6	samples crumbled
E25-50	Yes	> 10	4	hard - smooth
E25-60	Yes	> 10	8	friable - smooth
E25-70	Yes	> 10	4	very friable - smooth
E25-80	Yes	> 10	4	very friable - smooth
E25-90	No	1.5	20	samples crumbled
E30-50	Yes	> 10	4	soft - smooth
E30-60	No	3.5	8	friable - smooth
E30-70	No	2	12	samples crumbled
E30-80	No	1	16	samples crumbled
E30-90	No	1	16	samples crumbled

Beside emulsions E25-90, which could be only superficially polymerised to a depth of 1.5 mm, the rest of the samples obtained from emulsion templates stabilised with 25 vol.% surfactant concentration were smooth with no pores visible to the naked eye (Figure 4-11). An increased friability of the polyHIPE monoliths was observed when templates with a higher internal phase

volume ratios were used as template. Thus, additional care was needed to demould the porous monoliths from the containers in order to avoid fracture or other damage.

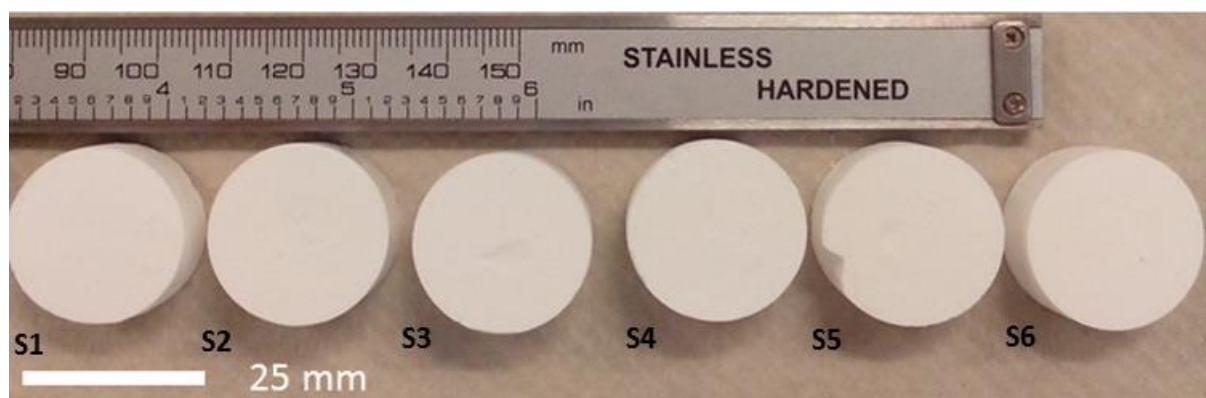


Figure 4-11. Monoliths produced by polymerisation of emulsion templates E25-60. The monoliths were friable with no visible pores to the naked eye. The sample S5 was replaced because of surface defects.

In the case of emulsion templates stabilised using a surfactant concentration of 30 vol.%, mechanically weak monoliths that easily broke during demoulding were obtained after polymerisation (Figure 4-12). This can be explained by the plasticising effect of the surfactant.¹⁸⁷⁻¹⁸⁸ Superficial polymerisation was also observed in all samples except for monoliths produced by polymerisation of emulsion templates E30-50. Only at low internal phase volume ratio, emulsions were transparent allowing the UV light to penetrate and polymerise the entire monolith. When emulsion templates with internal phase volume ratio above 50 % were used, only a few millimetres of the sample surface could be polymerised (Figure 4-12). Again, the reduction of the cure depth with increasing internal phase volume ratios can be explained by a decrease of the UV transparency of the emulsion templates with increasing amounts of dispersed phase.



Figure 4-12. Monoliths produced by polymerisation of emulsion templates E30-60. Only a polymerised layer between 3 - 4 mm was formed after UV irradiation for approximately 20 min. All samples were discarded.

In an attempt to increase the cure depth, the samples stabilised with 30 vol.% surfactant were additionally exposed to UV light ten times on each side without any visible improvement in the cure depth. We found that the optimum surfactant concentration needed to produce a porous interconnected monoliths with the best mechanical properties was around 15 vol.%. The use of higher surfactant concentrations proved to be detrimental for both Young's modulus and crush strength, which can be explained by the plasticising effect of the surfactant remaining in the pore walls. Moreover, the use of emulsion templates with higher surfactant concentrations promoted the formation of small but numerous pore throats in the pore walls, which could undermine the load bearing capacity of the resulting polyHIPEs.^{49, 291} The formulations providing the best results had an internal phase volume ratio between 50 and 60 %, which determined the final density of the porous polymer and its ability to support compressive forces.

Influence of emulsification energy on mechanical properties of monoliths produced by emulsion templating

The stability of an emulsion is influenced by the droplet size. This is due to the fact that the dispersed phase has in most cases a different density compared to the continuous phase, so a net gravitational force acts on the droplets causing creaming or sedimentation of the droplet phase. The droplets move through the continuous phase at a velocity proportional to the density difference between the two phases and the droplet size as defined by Stoke's Law:

$$\frac{dx}{dt} = \frac{2a^2(\rho_2 - \rho)g}{9\eta} \quad \text{Equation 4-1}$$

where, g is the acceleration due to gravity, $(\rho_2 - \rho)$ the difference in densities of the liquids, η the dynamic viscosity of the continuous phase and a the droplet radius. Increasing the amount of energy provided during emulsification will increase the interfacial area between the two phases by reducing the overall droplet size and, therefore, increasing emulsion stability. Emulsion templates stabilised with 10 vol.% or less surfactant were only stable for a short period of time, which was insufficient to produce suitable samples for compression testing. In an attempt to improve the stability of the emulsion templates, the energy input during emulsification was increased. A more stable emulsion will give us the opportunity to fill the mould with emulsion and polymerise the entire monolith before destabilisation of the

emulsion takes place. In order to increase the energy input the duration of stirring was increased from 5 to 10 min. The effect of a higher energy input in the emulsion E15-70 was significant and the stability of the emulsion was extended from a few minutes to more than 36 h. In the case of emulsion E10-70, the amount of time before any evidence of phase separation was detected increased from 2 to approximately 10 min. This small increase in stability was enough to produce suitable samples for mechanical testing. In the case of emulsion E10-50, increasing the stirring time to 10 min was insufficient to produce a stable emulsion. Another attempt was done increasing the stirring speed from 500 rpm to 1000 rpm while keeping the stirring time constant at 5 min, in this case a suitable sample could be obtained. The porous monoliths obtained from formulation E10-50 were hard but after the sample was fractured a few pores with a size 1 mm could be seen by the naked eye. The results of the compression tests performed on the monoliths produced after polymerisation of the emulsion templates is presented in Tables 4-6 and 4-7.

Table 4-6. Young's modulus of poly(MMA-co-EGDMA) foams produced from emulsion templates with different surfactant concentrations and internal phase volume ratio. Values inside dotted lines were measured for samples from emulsion templates stirred at 500 rpm for 10 min while values inside dashed lines were measured for samples from emulsion templates stirred for 5 min at 1000 rpm. The applied energy was 0.24 and 0.48 kJ/m³ respectively.

		Young's modulus [MPa]				
Surfactant concentration [vol. %]	30	12.6 ± 4.9	Only the surface of the samples could be polymerised			
	25	39.2 ± 2.6	26.6 ± 7.3	22.8 ± 2.9	8.5 ± 2.6	
	20	80.1 ± 8.9	70.3 ± 2.8	48.5 ± 13.2	12.8 ± 2.2	
	15	186.5 ± 10.6	137.6 ± 10.6	57.1 ± 9.2	24.5 ± 7.3	7.9 ± 1.0
	10	149.1 ± 18.4	125.8 ± 13.3	23.2 ± 2.5	Phase separation zone	
	5					
		50	60	70	80	90
		Internal phase volume ratio [%]				

Samples produced by polymerisation of emulsion templates E10-50 stirred at 500 rpm for 10 min (energy input of 0.48 kJ/m³) had a Young's modulus of 149.1 ± 18.4 MPa and a crush strength of 10.1 ± 0.9 MPa. This formulation was stabilised using the lowest surfactant concentration possible and, therefore minimising the plasticising effect of the surfactant in

the pore walls. The results obtained are mostly determined by the foam density, which was the highest because of the low amount of internal (templating) phase and represented 50 vol.% of the emulsion.

Table 4-7. Crush strength of poly(MMA-co-EGDMA) foams produced from emulsion templates with different surfactant concentrations and internal phase volume ratio. Values inside dotted lines were measured for samples from emulsion templates stirred at 500 rpm for 10 min while values inside dashed lines were measured for samples from emulsion templates stirred for 5 min at 1000 rpm. The applied energy was 0.24 and 0.48 kJ/m³, respectively.

		Maximum Stress - Crush strength (MPa)				
Surfactant concentration [vol. %]	30	1.0 ± 0.2	Only the surface of the samples could be polymerised			
	25	2.6 ± 0.3	1.4 ± 0.3	1.1 ± 0.1	0.4 ± 0.1	
	20	3.9 ± 0.5	3.8 ± 0.4	2.1 ± 0.4	0.9 ± 0.1	
	15	8.4 ± 0.3	8.3 ± 0.3	4.5 ± 0.3	1.1 ± 0.2	0.6 ± 0.1
	10	10.1 ± 0.9	5.0 ± 0.5	1.8 ± 0.3		
	5	Phase separation zone				
		50	60	70	80	90
		Internal phase volume ratio [%]				

Despite the higher energy input used to produce the emulsion templates with reduced surfactant concentrations from which macroporous polymer monoliths were produced, no significant improvement in the Young's modulus was observed (Figures 4-13 and 4-14). Overall, samples produced from emulsion templates stabilised with a surfactant concentration between 10 and 15 vol.% showed the highest values measured. In the case of emulsions E10-80, E10-90 and emulsion templates with a surfactant concentration of 5 vol.%, it was not possible to produce stable emulsions by increasing the energy input.

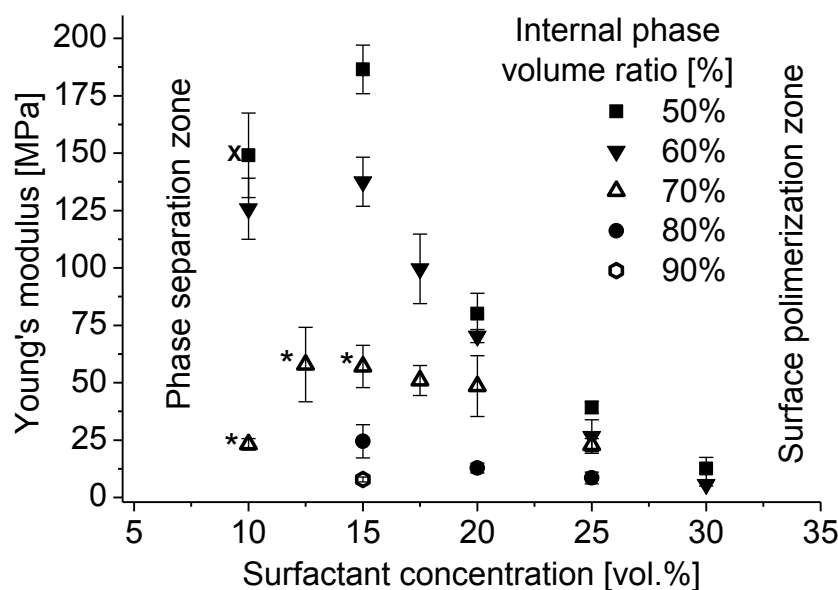


Figure 4-13. Young's modulus of poly(MMA-co-EGDMA) porous foams produced by polymerisation of emulsion templates prepared with increasing energy input during emulsification. All samples were emulsified with an energy input of 0.24 kJ/m^3 , except samples indicated with (*) 0.48 kJ/m^3 and (x) 1.92 kJ/m^3 . These samples required additional emulsification energy to form suitable samples for compression test.

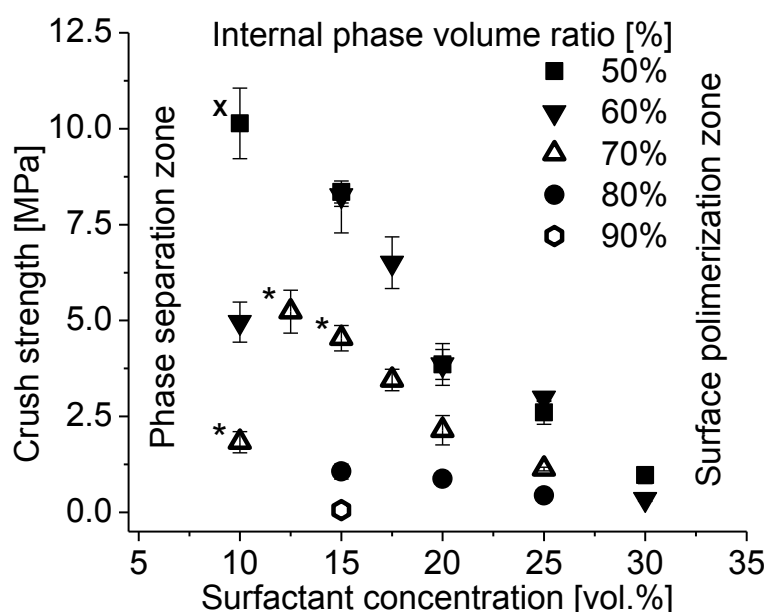


Figure 4-14. Crush strength of poly(MMA-co-EGDMA) porous foams produced by polymerisation of emulsion templates prepared with increasing energy input during emulsification. All samples were emulsified with an energy input of 0.24 kJ/m^3 , except samples indicated with (*) 0.48 kJ/m^3 and (x) 1.92 kJ/m^3 . These samples required additional emulsification energy to form suitable samples for compression test.

Several examples in the literature reported the positive influence of a hierarchical pore size distribution on the mechanical properties of foams with similar porosities.^{21, 49, 171} Moreover, previous work of our group showed that pore size and pore throat diameter of polyM/HIPes can be predicted and also controlled by controlling the energy input during emulsification of the emulsion templates.¹⁷⁴ Supported by these previous findings, it was decided to vary the use different energy input during emulsification and analyse its influence on the mechanical properties of the foams produced.

Influence of emulsification energy on the morphology of polyMIPes produced by emulsion templating

Emulsion templates E15-60 were used for further study as they showed good stability after emulsification with relatively low energy inputs of 0.24 kJ/m^3 (5 min stirring at 500 rpm) and could be stabilised with low surfactant concentrations (15 vol.%). Additionally, from all the foams created using emulsion templates with an internal phase volume ratio of 60 %, monoliths produced using this formulation after polymerisation had the highest crush strength ($8.3 \pm 0.3 \text{ MPa}$). Different emulsion templates with this formulation (E15-60) were produced by varying stirring time and speed used during emulsification and, therefore, the energy applied (E_v). Monoliths created after polymerisation of the different emulsion templates are shown in Figure 4-15. Attempts to create stable emulsion templates with an energy input of 0.19 kJ/m^3 (4 min stirring at 500 rpm) were not successful, every time a few seconds after the stirring stopped phase separation was visible inside the reactor.

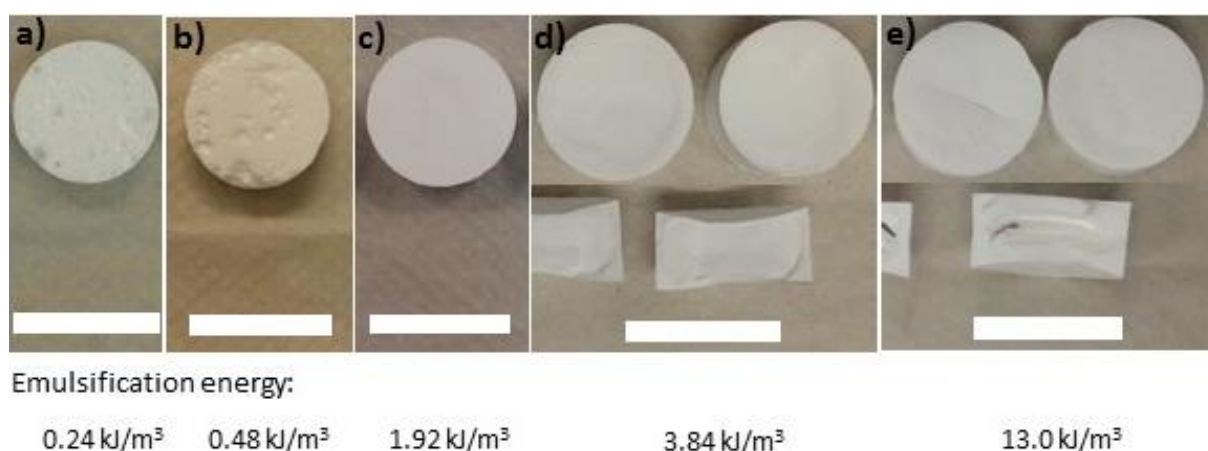


Figure 4-15. Photographs of monoliths obtained from emulsion templates produced with different energy inputs during emulsification. The emulsification energy used increases from left to right. All scale bars represent 25 mm.

In the case of emulsion templates created with an energy input during emulsification of 0.24 kJ/m^3 , the monoliths created after polymerisation contained a few pores of approximately 1.5 mm (Figure 4-15a). When the energy input during emulsification was increased from 0.24 to 0.48 kJ/m^3 , polyMIPs with a more homogeneous morphology were obtained after polymerisation. The samples produced had a few pores between 1 and 2 mm (Figure 4-15b). When the energy input was increased to 1.92 kJ/m^3 the monoliths obtained after polymerisation of the emulsion templates had a homogeneous internal morphology with no pores visible to the naked eye (Figure 4-15c). Monoliths with the same visual aspect were produced from emulsion templates with an energy input of 3.8 kJ/m^3 . When the energy input during emulsification was increased to 13 kJ/m^3 , it was not possible to achieve a complete polymerisation of the emulsion templates even after the samples were exposed to UV light for 10 min on each side. After fracturing the monoliths it could be observed that a superficial layer of approximately 2.5 mm was polymerised while the rest of the sample remained liquid, leading to a large void after purification (Figure 4-15e). As discussed before (Table 4.5), a smaller droplet size product of a higher energy input seems to reduce the transparency of the emulsion templates and, therefore, the penetration of UV light. The effect of increasing the emulsification energy on the mechanical properties of the polymerised monoliths was studied. After the energy input was increased from 0.24 to 0.48 kJ/m^3 , a significant reduction in Young's modulus from 137.5 ± 10.6 to $65 \pm 9.8 \text{ MPa}$ was observed (Figure 4-16).

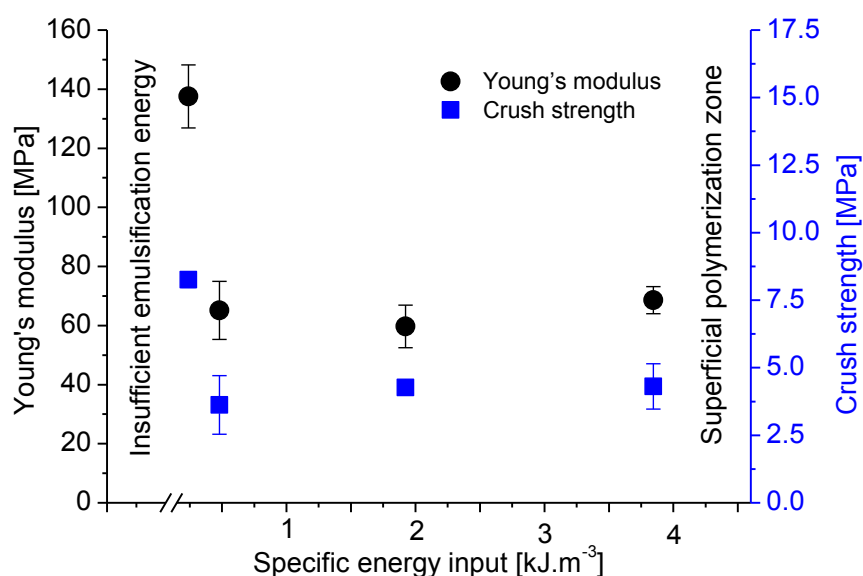


Figure 4-16. Young's modulus and crush strength of monoliths produced using emulsion templates (E15-60) emulsified with increasing energy input.

Additionally, a similar decrease of more than 50 % in the crush strength of the samples was observed. Further increasing in the emulsification energy of the emulsion templates (from 0.48 to 3.8 kJ/m³) led to monoliths with no significant variation in Young's modulus, only a slight increase in crush strength from 3.6 ± 1.1 to 4.3 ± 0.7 MPa was observed. So far every increase in energy input above the minimum amount of energy needed to produce stable emulsion templates (0.24 kJ/m³) had a negative effect on the Young's modulus and crush strength of the samples produced after polymerisation (Table 4-11).

Table 4-11. Properties of macroporous monoliths produced by polymerisation of emulsion templates (E15-60) with increasing energy input during emulsification.

Specific energy input [kJ/m ³]	Stirring speed [rpm]	Stirring time [min]	Young's modulus [MPa]	Crush strength [MPa]	Porosity [%]	Pore size [μm]	Pore throat size [μm]
0.19	500	4	Phase separation				
0.24	500	5	137.5 ± 10.6	8.3 ± 0.3	71 ± 2	55.5 ± 62.8	3.0 ± 1.2
0.48	500	10	65.1 ± 9.8	3.6 ± 1.1	75 ± 1	50.5 ± 98.4	2.2 ± 1.6
1.92	1000	5	59.7 ± 7.2	4.3 ± 0.2	73 ± 1	4.5 ± 2.9	0.8 ± 0.3
3.84	1000	10	68.6 ± 4.6	4.3 ± 0.7	75 ± 2	3.3 ± 2.2	1.0 ± 0.3
13.0	1500	10	Only the surface of the samples could be polymerised		72 ± 1	1.8 ± 0.9	0.5 ± 0.2

No significant variations in the porosity of the monolithic samples were revealed after testing. However, the average pore and pore throat sizes showed a dramatic increase in polyMIPes produced by polymerisation of emulsion templates prepared with low energy input during emulsification (Table 4-11). The internal structure of the polymerised monoliths is shown in Figure 4-17. We can clearly observe the reduction in pore size when higher energy inputs were used during the preparation of the emulsion templates from which the polyMIPes were produced. The pore size of polyMIPes obtained after polymerisation of emulsion templates created with an energy input of 0.24 kJ/m³ was 55.5 ± 62.8 μm. This samples, which had the highest Young's modulus and crush strength of all polyMIPes tested, had a broad pore size distribution and only a very few pore throats with a size of 3.0 ± 1.2 μm (Figure 4-17a). When the formulation E15-60 was emulsified with an energy input of 0.48 kJ/m³, the polyMIPE monoliths produced after polymerisation of the resulting emulsion had a pore size of 50.5 ± 98.4 μm. Pore throats with a size of 2.2 ± 1.6 μm were more frequent (Figure 4-17b).

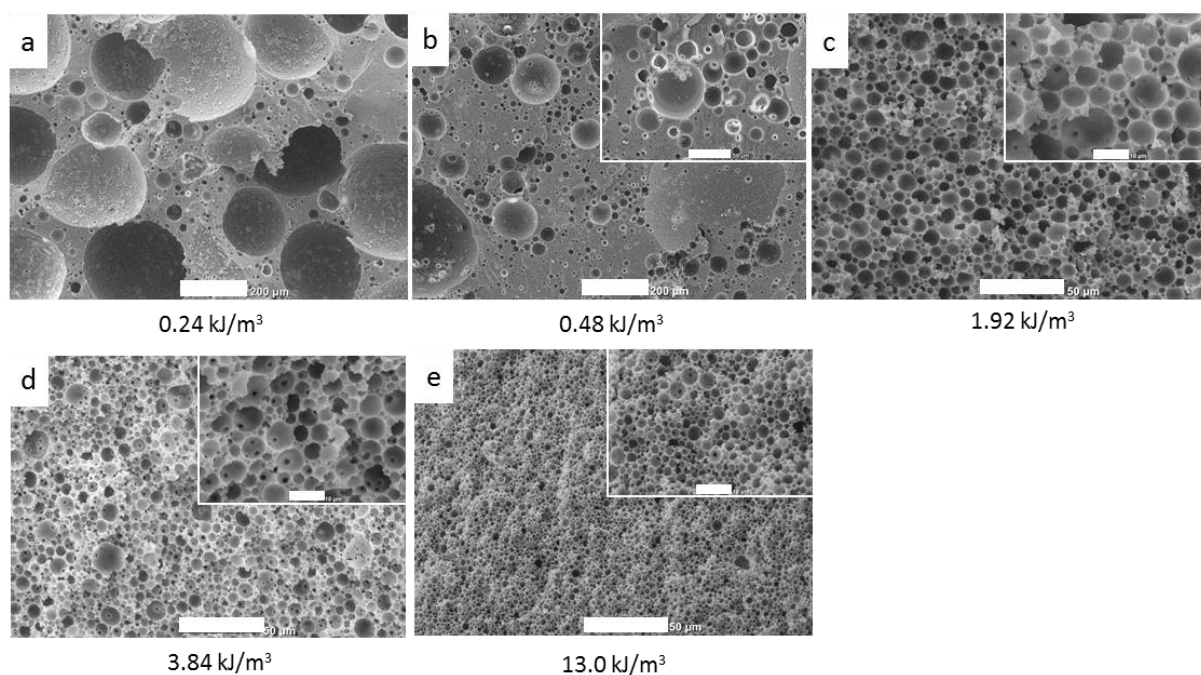


Figure 4-17. SEM images of polyHIPEs prepared by polymerisation of emulsion templates E15-60 prepared with increasing energy input. In images a) and b) scale bars represent 200 μm while the scale bar in the insert represent 50 μm . The scale bar in images c-e) represents 50 μm while the bar in the inserts represents 10 μm .

An energy input of 1.92 kJ/m^3 during the emulsification process led to the formation of polyMIPE monoliths with a decrease of almost 90 % in average pore size after polymerisation. An energy input during emulsification of 13 kJ/m^3 , achieved by stirring the emulsion templates for 10 min at a stirring speed of 1500 rpm, led to the formation of samples with even smaller pore and pore throat sizes, $1.8 \pm 0.9 \mu\text{m}$ and $0.5 \pm 0.2 \mu\text{m}$, respectively (Figure 4-17e). The reduction in pore size is related to the amount of energy needed to break the water droplets. A low energy input during the emulsification process created emulsions with a broad droplet size distribution while higher energy input formed emulsions with smaller droplets and a narrower droplet size distribution. Emulsion templates with a narrow droplet size distribution led to a more homogeneous pore structure after polymerisation.

In the case of emulsions produced with an energy input of 13 kJ/m^3 , only the surfaces of the emulsion templates could be polymerised and, therefore, compression tests could not be performed. Apparently, for this specific emulsion template formulation, a droplet size of $1.8 \pm 0.9 \mu\text{m}$ reduced the UV transparency of the emulsion templates preventing complete polymerisation of the monolithic samples.

Effect of higher emulsification energy on the mechanical properties of polyMIPEs

The pore size and size distribution are believed to play an important role in the mechanical properties of porous polymers. It was observed that polyHIPEs with a broad pore size distribution, and therefore, a more efficient packing of the pores had improved mechanical strength.¹⁷¹ The samples obtained after polymerisation of emulsion templates created with an energy input of 0.24 kJ/m^3 showed had a broad pore size distribution with an average pore size of $55.5 \pm 62.8 \text{ }\mu\text{m}$ and only a very few pore throats with a size of $3.0 \pm 1.2 \text{ }\mu\text{m}$ (Figure 4-16a). This samples had the highest Young's modulus and crush strength of all polyMIPEs of this series.

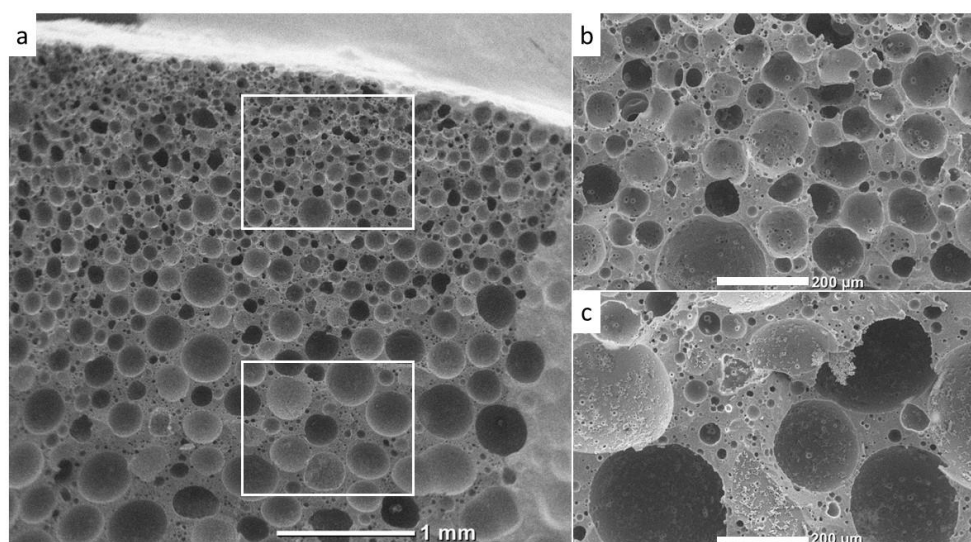


Figure 4-16. SEM images of monoliths obtained from emulsion templates E15-60 (energy input 0.24 kJ/m^3). The scale bar in images b and c represents $200 \text{ }\mu\text{m}$

The broad pore size distribution, with a standard deviation higher than the average pore size indicates an internal pore structure influenced by early coalesce due to the poor stability of the emulsion. In SEM images of the internal structure of the foams, a gradient in pore size can be observed (Figures 4-16 b and c). The monoliths used for compression tests had bigger pores in the inner part of the sample and smaller pores close to the borders. The average pore size at the top of the porous monolith (Figure 4-16b) was $53.8 \pm 40.2 \text{ }\mu\text{m}$ while closer to the sample centre (Figure 4-16 c), the pore size was $57.5 \pm 80.9 \text{ }\mu\text{m}$. While both morphologies have a similar average pore size, the standard deviation was almost double. The gradient in pore size could be caused by a rapid polymerisation of the emulsion templates at the surface, and as the distance from the surface increases polymerisation requires more time, allowing coalescence of the emulsion before the gel point is reached. The internal pore morphology is

better represented by the pore size distribution (Figure 4-17) than the average pore size and standard deviation.

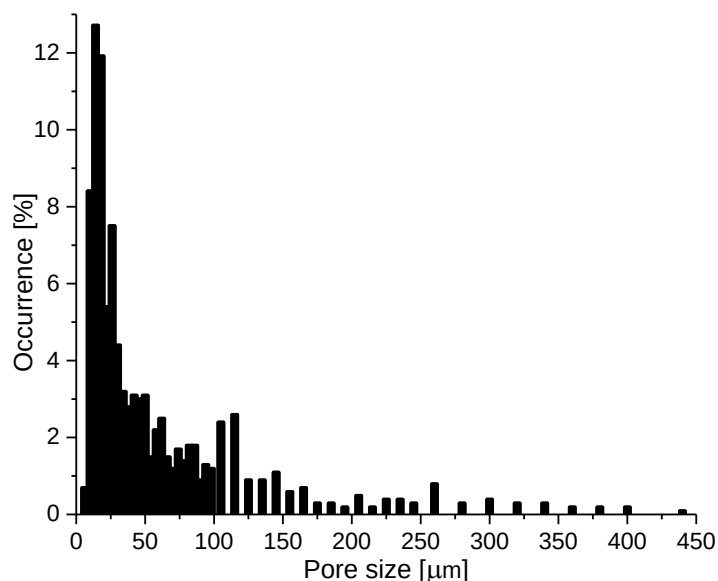


Figure 4-17. Pore size distribution of polyHIPE monoliths produced after polymerisation of emulsion templates E15-60 (image a) emulsified with an energy input of 0.24 kJ/m^3 (stirring for 5 min at 500 rpm).

The evidence confirms that it is not only the pore size distribution and pore throat size that define the mechanical performance but also the quantity of pore throats, because the pore throats act as defects reducing the bending stiffness of the polymer walls of foams as reported in detail by Luo et al.¹⁸⁶

4.3.5 Thermal stability of poly(MMA-co-EGDMA) macroporous polymers

Samples from polymerised emulsion templates with an internal phase volume ratio of 60 % stabilised by different surfactant concentrations were prepared according to section 3.4.3. The weight loss as function of temperature is shown in Figure 4-18a. A single stage decomposition curve was visible for all samples. A weight loss of approximately 2 % can be observed in all samples corresponding to the isotherm used at $120 \text{ }^\circ\text{C}$ for 15 min. This weight loss can be explained due to desorption of physically absorbed water. All polyMIPes showed a significant weight loss starting approximately at $175 \text{ }^\circ\text{C}$. The thermal degradation temperature, defined as the temperature at a weight loss of 50 %, was around $276 \pm 6 \text{ }^\circ\text{C}$,

comparable with degradation temperatures of poly (methacrylate) HIPEs with similar compositions.²⁹²⁻²⁹³

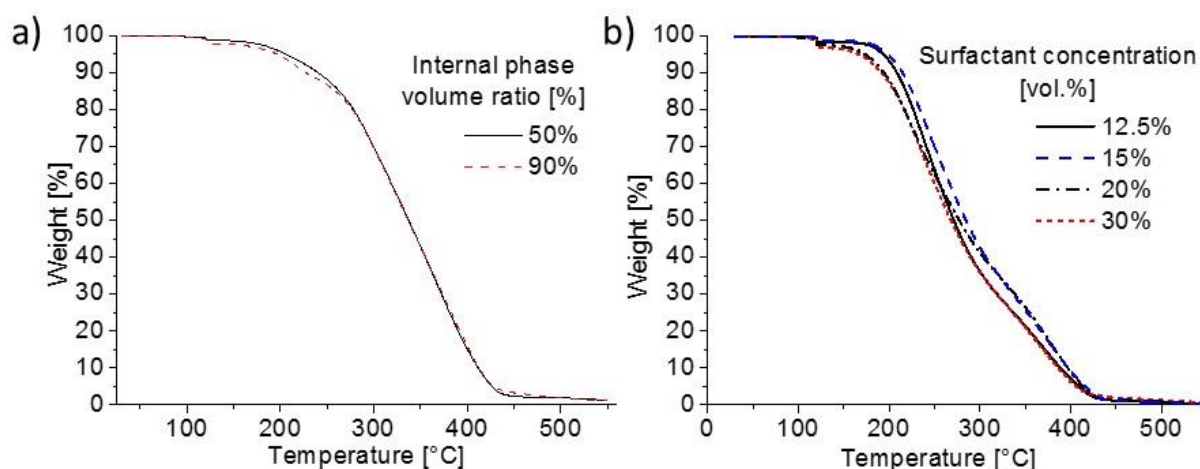


Figure 4-18. Thermo gravimetric analysis of macroporous polymers obtained by polymerisation of: a) emulsion templates with 60 % internal phase volume ratio and different surfactant concentrations b) emulsions stabilised with 15 vol.% of surfactant and different internal phase volumes

It was observed that polyMIPes produced from emulsion templates containing increasing amounts of surfactant had a more pronounced weight loss, which is probably due to residual amounts of surfactant present in the porous structure after purification and drying. At 500 °C almost complete degradation had occurred and only less than 1.5 % of the original sample remained. This residue could be due to trace amounts of plasticisers or inorganic impurities not removed during purification. In the case of polyMIPes with different densities, produced from emulsion templates with internal phase volume ratios between 50 and 90 % (Figure 4-18b), no significant difference was observed in the initial decomposition temperature.

4.4 Summary

Macroporous beads were produced from W_1 /MMA-EGDMA emulsion templates by sedimentation polymerisation. The boundaries between beads with a close celled and interconnected pore structure were identified. However, beads with a close celled structure can only be produced when low amounts of surfactant are used to stabilise the emulsion templates, which had a negative impact in emulsion stability. Emulsions with reduced stability resulted in catastrophic phase separation or beads and monoliths with a broad size dispersion

after polymerisation. The minimum amount of surfactant and energy input suitable to produce stable emulsion templates was 15 vol.% and 0.24 kJ/m³.

Monolithic samples with a thickness of approximately 12 mm were produced by UV photopolymerisation. Monoliths produced by polymerisation of emulsion templates stabilised with a surfactant concentration of 15 vol.% had the highest Young's modulus of all samples tested. The use of larger surfactant concentrations in the emulsion templates led to reduced mechanical properties, which can be explained due to a plasticising effect of the surfactant on the pore walls and the formation of numerous pore throats debilitating the load bearing capacity of the material. As expected, polymerisation of emulsion templates with increasing internal phase volume ratios showed reduced mechanical properties due to a reduction in foam density.

The amount of surfactant used not only influenced the stability of the emulsions over time but also affected the ability to photopolymerise the emulsion templates. Superficial polymerisation was observed in emulsions containing surfactant concentrations higher than 25 vol.%. High surfactant concentrations or energy inputs during emulsification promoted the formation of emulsion templates with smaller droplets, which increased UV light scattering and reduced polymerisation depth.

Mechanical properties were tuned by adjusting the surfactant concentration used to stabilise the emulsion templates, the internal phase volume ratio or simply controlling the energy input used in the emulsification process. Higher stirring rates led to weaker mechanical properties due to formation of thinner pore walls that have a reduced buckling resistance.

The macroporous poly(MMA-co-EGDMA) polymers produced were thermally stable until a temperature of 150-175 °C was reached and degradation temperature was observed around 270°C.

Chapter 5. Effect of initiation locus on pore structure of macroporous beads produced by sedimentation polymerisation of ($W_1/O/W_2$) multiple emulsions

5.1 Introduction

Porous polymer beads with controlled size and size dispersion are attractive as delivery systems of active ingredients for a wide range of applications. They can be used in the Oil & Gas and personal care industries, and as additive in composite materials to deliver a healing agent, which will allow to seal cracks and restore mechanical properties.¹⁴ Polymerisable multiple emulsion templates can be used to encapsulate active ingredients within macroporous beads, if the active ingredient is present in the dispersed phase (W_1) of the emulsion. Encapsulation of the active ingredient can be achieved by polymerising the organic minority monomer phase of W_1/O emulsion droplets that are stable throughout the polymerisation process, “entrapping” the active compound inside the structure of the beads.³⁴ In order to avoid diffusion, permeation, or both through the oil phase into the secondary aqueous phase (W_2) and retain the active ingredient, a rapid polymerisation is desirable. Using photopolymerisation, instead of a classical thermal polymerisation, to cure the monomer phase of $W_1/O/W_2$ emulsion template droplets allows for rapid solidification of the oil membrane increasing the encapsulation efficiency. Once the encapsulated compound is trapped within the porous structure of the beads, the effectiveness of the encapsulation will be determined by the permeability of the polymeric layer formed around the active ingredient. Usually, the use of molecular surfactants to stabilise W_1/O emulsion droplets results in porous beads with interconnecting pore throats typically in the order of 1 μm , which provides connectivity not only between the internal pores but also to the surrounding environment. Macroporous beads with a dense surface film or “crust” and an interconnected internal pore structure are ideal to contain and preserve the active substance inside the bead for a certain period of time and to control its release into the environment when predefined conditions are met, for example when the surface of the bead is cracked open. The closed surface protects and contains the active substance inside the bead while the interconnected pore structure allows for complete release of the encapsulated ingredients to the

environment after the bead is crushed or the surface damaged. Reducing the interconnectivity of the pore walls inside macroporous polymer beads may prevent early degradation or release of the encapsulated active compounds, increasing the shelf-life of the active ingredient. A low pore interconnectivity in macroporous materials produced by emulsion templating can be obtained using particle stabilised or Pickering emulsions.⁶⁴ Although the materials produced tend to have an internal close celled structure, Gurevitch and Silverstein^{65, 294-295} showed that is possible to influence the pore interconnectivity of acrylate based Pickering polyHIPEs by using different radical initiators, leading to the formation of an interconnected pore network. When using surfactant stabilised emulsions several approaches can be used to reduce the pore interconnectivity. An effective method is to reduce the amount of surfactant used to stabilise the emulsions along with the internal phase volume ratio, both options led to materials with thicker polymer pore walls. But these two alternatives have also drawbacks; reducing the amount of surfactant used to stabilise the emulsion template can result in a reduced stability of the emulsion, while lowering the internal phase volume ratio decreases the total volume available to encapsulate a compound. Another option to reduce interconnectivity is to change the location of the initiator used to initiate the polymerisation of the organic monomer phase of the emulsion template.²⁹⁶ A typical interconnected pore structure will be formed if an oil soluble initiator is used irrespectively of the surfactant employed to stabilise the emulsion templates. However, it is possible to significantly reduce pore interconnectivity or even produce a close celled pore structure if the polymerisation of the organic phase of the emulsion is initiated in the aqueous phase by use of water soluble initiators, such as redox initiator systems or potassium peroxodisulfate ($K_2S_2O_8$) in the dispersed phase of the emulsion (W_1).²⁹⁶ Viswanathan et al.²⁹⁷ proposed that the location of the initiator plays a major role in the formation of interconnecting pores. They polymerised W/O emulsion templates where the initiator potassium peroxodisulfate ($K_2S_2O_8$) was present in the dispersed aqueous phase (W_1) and AIBN was used in the continuous oil phase. In their work, the formation of interconnecting pores was explained by the location of the formed radicals in the emulsion. When the initiator was present in the water phase, polymerisation started at the W_1/O interface advancing to the bulk and forming rigid polymer walls between droplets. This effect prevents coalescence of neighbouring water droplets that cause formation of interconnecting pore throats. Krajnc et al.¹⁶⁹ compared the internal morphology of porous polymers produced by polymerisation of surfactant stabilised W_1/O

emulsion templates based on glycidyl methacrylate and ethyleneglycol dimethacrylate (GMA-EGDMA) as organic phase. After using the thermal initiator system ammonium persulfate/*N,N,N',N'*-tetramethylethylenediamine (APS/TEMED) dissolved in the dispersed aqueous phase and α,α' -azoisobutyronitrile (AIBN) in the continuous organic phase they proposed that the formation of interconnecting pore throats in the polymer pore walls was influenced by the kinetics of radical formation. A reduction in pore throat size of almost 75% was achieved when the initiator system APS/TEMED was used instead of AIBN. They postulated that when using water soluble thermal initiator systems, the formation of free radicals and hence the transition to the gel point occurs faster, resulting in locking the droplets of internal phase before destabilisation occurs, which results in the formation of smaller polyhedral pores with a reduced degree of pore interconnectivity.

Influence of additives to the secondary aqueous phase (W_2) and polymerisation initiation locus on bead morphology

The permeability of the bead surface should be influenced by the “skin” of the bead, whose formation is influenced by the stability of the O/ W_2 droplet interface during polymerisation. The emulsion droplet interface (O/ W_2) is usually stabilised using hydrophilic emulsifiers with a high HLB value dissolved in the secondary aqueous phase (W_2).⁹⁴ The interaction of hydrophilic and lipophilic emulsifiers that occur on the O/ W_2 interface and the chemical structure of the emulsifier will influence the stability of the W_1 /O/ W_2 multiple emulsion. The hydrophilic emulsifier used should not only be adequate to stabilise the O/ W_2 interface but also needs to be compatible with the properties and amounts of the lipophilic surfactant used to stabilise the W_1 /O emulsion.¹⁰⁸ For example, macroporous beads were produced from W_1 /styrene-divinylbenzene emulsion templates after injection of the emulsion into a secondary aqueous phase (W_2) composed of a 3.5 wt.% solution of poly (diallyl dimethyl ammonium chloride) (PDDAC) as stabiliser.²¹⁵ The emulsion contained the water soluble initiator potassium peroxodisulfate ($K_2S_2O_8$) dissolved in the dispersed phase of the emulsion (W_1) forming beads with an open skin and interconnected pore structure after polymerisation. In case of emulsions containing acrylates in the organic phase, poly(vinyl alcohol) (PVA) alone³⁴ or in combination with surfactants, such as sodium dodecyl sulphate (SDS),²⁹⁸ *t*-octylphenoxypolyethoxyethanol (Triton X-100)²⁷¹ or octylphenol ethoxylate (Triton X-405)²⁹⁹ were proven to be effective stabilisers when dissolved in the outer aqueous phase

(W_2) of multiple emulsions. PVA is commonly used as stabiliser in the production of nano- and microbeads since it increases the viscosity of the external carrier phase and acts to reduce interfacial tension at the droplet surface, reducing droplet coalescence.³⁰⁰⁻³⁰¹ More precisely, PVA and Triton X-405 were used to stabilise W_1/O emulsion droplets for the production of beads through suspension polymerisation³⁰²⁻³⁰⁴ and also in the aqueous phase of O/W_1 emulsions.²⁷³ However, the influence of a secondary aqueous phase (W_2) containing PVA and Triton X-405 or other components on the surface structure of the beads produced after polymerisation of W_1/O emulsion droplets was not yet studied. Moreover, it may be possible to modify the permeability of the bead surface by using a secondary aqueous phase (W_2) with a lower concentration of $CaCl_2$ electrolyte than the internal dispersed phase (W_1) of the emulsion. The $CaCl_2$ concentration gradient between W_1 and W_2 phases may promote a controlled destabilisation of the O/W_2 interface due to diffusion of H_2O into the internal aqueous phase (W_1). Furthermore, the use of an initiator located in the secondary aqueous phase may result in porous beads with a closed surface and interconnected internal bead pore structure after polymerisation. The initiation of polymerisation from the internal dispersed phase (W_1) of W_1/O HIPE templates led to polyHIPEs with a closed celled pore structure.²⁹⁶ Such an approach to produce macroporous beads with a closed surface and interconnected pore structure is described in this chapter. The initiation locus was varied between the water dispersed phase (W_1), the oil phase (O) and the secondary aqueous phase (W_2) using the initiators bis(2,4,6-trimethylbenzoyl) phenylphosphine oxide (Irgacure 819), 2-hydroxy-2-methyl-1-phenyl-1-propanone (Darocur 1173), 2,2'-azobis(2-methylpropionamidine) dihydrochloride (AAPH) and potassium persulfate (KPS) alone or combined in different concentrations. The initiator used in the organic phase was Darocur 1173, which was already proven to be successful for the development of an interconnected pore network. In the outer aqueous phase (W_2), the water soluble thermal initiator KPS was used. KPS was previously used in the dispersed phase of water/styrene-DVB emulsions to produce polyHIPEs with closed celled pore structures.²⁹⁶ This initiator has a half-life time of 202 h at 50°C, 60 h at 60°C and 8 h at 70°C,³⁰⁵ so similar temperatures were used for the carrier phase (W_2) with the objective to progressively increase the amount of radicals available for polymerisation. Additionally, in order to prevent destabilisation of the emulsion droplets due to the higher temperatures needed to initiate thermal polymerisation, a faster curing was attempted by using the photoinitiator Irgacure 819 dissolved in the secondary aqueous phase (W_2). Irgacure

819 is a solid UV photoinitiator commonly used in radical polymerisation and especially suited for white pigmented formulations. According to the manufacturer (Ciba a subsidiary from BASF SE, Ludwigshafen, Germany) a concentration between 0.5 and 1 wt.% is recommended for acrylate formulations. Irgacure 819 and Darocur 1173 showed the best results compared to other photoinitiators when used to initiate the polymerisation of acrylates using a wavelength of 365 nm.³⁰⁶ However, Darocur 1173 has absorption peaks at 245, 280 and 331 nm, while Irgacure 819 has peaks at 360, 365 and 405 nm.³⁰⁷ The absorption peaks of Irgacure 819 match the irradiation peak of our handheld UV light (UVP Blak-Ray B100AP) used to initiate the polymerisation of droplets better than Darocur 1173 (Figure 5-1). Moreover, Irgacure 819 has been also successfully used in the organic phase of high internal phase emulsions to initiate their polymerisation upon exposure to UV light.³⁰⁸

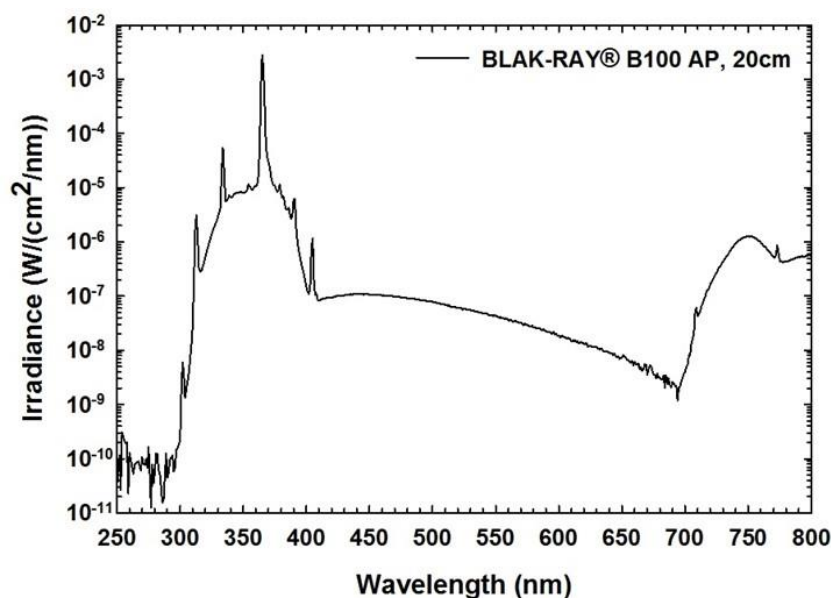


Figure 5-1. Spectral irradiance chart of the hand held UV light used (Blak Ray B-100 AP).³⁰⁹

Therefore, in this chapter we explored different alternatives for the production of macroporous beads with an interconnected internal pore structure but closed surface. The effect of the locus of polymerisation initiation and the initiator type on the surface and pore structure of the beads is described. Moreover, different components such as calcium chloride electrolytes with different concentrations, polyvinyl alcohol (PVA) and octylphenol ethoxylate (Triton X-405) were used in the secondary aqueous carrier phase (W_2) and their influence on the bead surface was studied.

5.2 Experimental

5.2.1 Materials

The monomer methyl methacrylate (MMA), crosslinker ethylene glycol dimethacrylate (EGDMA), calcium chloride dihydrate ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$), initiators potassium persulfate (KPS) and 2,2'-azobis(2-methylpropionamidine) dihydrochloride (AAPH) and the emulsifiers polyvinyl alcohol (PVA) with an average molecular weight of 30.000-70.000 g/mol, poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) MW = 2.800 g/mol (Pluronic L-81) and octylphenol ethoxylate (Triton X-405) were purchased from Sigma-Aldrich (Vienna, Austria). The photoinitiators 2-hydroxy-2-methyl-1-phenyl-1-propanone (Darocur 1173) and bis(2,4,6-trimethylbenzoyl) phenylphosphine oxide (Irgacure 819) were kindly donated by BTC Europe GmbH (Düsseldorf, Germany). All chemicals were used as received.

5.2.2 Preparation of the W_1/O emulsion templates and secondary aqueous phase (W_2)

The organic phase of all W_1/O emulsions prepared consisted of a mixture of MMA and EGDMA as monomer and crosslinker in a ratio of 60/40 (vol/vol). The surfactant Pluronic L-81 was dissolved in the monomers in a concentration of 15 vol.% with respect to the organic phase. Except indicated otherwise, the dispersed phase of all the emulsion templates (W_1) consisted of an aqueous solution containing 1.3 wt.% (13.2 g/L) of calcium chloride dihydrate ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$) as electrolyte in order to suppress Ostwald ripening. To prepare the emulsion templates, the continuous yet minority organic phase was mixed in a reactor vessel (glass, 250 mL volume) fitted with a glass paddle rod (2 blades, anchor shape) connected to an overhead stirrer Heidolph RZR 2102 Control (Heidolph Instruments GmbH, Schwabach, Germany) for 5 min at 500 rpm to achieve homogeneity. After preparation of the organic phase, the dispersed aqueous phase (W_1) was added dropwise keeping the stirring speed constant. Following addition of the electrolyte, stirring continued for another 10 min to obtain a homogeneous emulsion. The total combined volume of continuous and dispersed phase was kept constant at 50 mL in order to apply a similar energy input to all emulsion templates produced. To prepare the secondary aqueous phase (W_2), different amounts of initiators and/or calcium chloride dihydrate ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$) were dissolved in 150 mL of distilled water in a sealed glass vessel using a magnetic stirrer (IKA RCT basic, IKA Ltd, Oxford, England) for a period of 20 h. The glass vessel used to stir the solution containing the initiator was completely covered with aluminium foil in order to avoid premature decomposition. The locus of initiation in the

emulsion templates was varied between the dispersed phase (W_1), the oil phase (O) and the secondary aqueous phase (W_2). The photoinitiator Darocure 1173 was dissolved in the organic phase of the emulsion templates (O-DAR beads) and in the secondary aqueous phase (W_2 -DAR beads) in order to initiate polymerisation. Additionally, beads (W_2 -IRG) were also produced by polymerisation of emulsion template droplets dispersed in the secondary aqueous phase (W_2) in which the photoinitiator Irgacure 819 was dissolved in order to initiate polymerisation at the W_2/O interface. Also, beads were produced by polymerisation of W_1/O emulsion template droplets initiated simultaneously from the organic phase (O) and the secondary aqueous phase (W_2). This was achieved by dissolving the photoinitiator Darocure 1173 in the organic phase of the emulsion and the water soluble initiator KPS into the secondary aqueous phase (W_2), leading to beads (OW_2 -DARKPS) after polymerisation. Moreover, beads (W_1 -AAPH) were produced by polymerisation of emulsion template droplets containing the water soluble photoinitiator AAPH dissolved in the dispersed phase of the emulsion (W_1). The dispersed aqueous phase (W_1) of the emulsion templates was produced by dissolving AAPH in an 1.3 wt.% $CaCl_2$ aqueous solution until a concentration of 12.3 mmol/L was reached. In an attempt to produce beads with thicker polymer walls promoting the formation of a closed pore structure, the emulsion internal phase volume ratio was reduced from 70 % to 60 %. Additionally, beads (OW_1 -DARAAPH) were produced using the photoinitiators Darocure 1173 dissolved in the organic phase of the emulsion (O) and AAPH in the dispersed phase of the emulsion (W_1). A summary of all formulations used, including the concentration and location of the different initiators is given in Table 5-1. The nomenclature used to name the formulations has two parts separated by a hyphen. The first part refers to the location of the initiator in the emulsion while the second part indicates the initiator used. If we take for example the code of formulation W_2 -DAR, in this case the polymerization was started from the secondary aqueous phase (W_2) and the initiator used was Darocur 1173.

Table 5-1. Summary of the nomenclature and formulations of the emulsion template used.

Formulation code	Internal phase volume ratio [%]	Initiator used	Location of the initiator ($W_1/O/W_2$)	Initiator concentration [mmol/L]	Carrier phase used ^a (W_2)
O-DAR-1	70	Darocur 1173	O	156	IP 1.3%
O-DAR-2	70	Darocur 1173	O	156	IP 0.5%
O-DAR-3	70	Darocur 1173	O	156	DW
O-DAR-4	70	Darocur 1173	O	156	PVA + Triton
W_2 -DAR-1	70	Darocur 1173	W_2	194	DW
W_2 -DAR-2	70	Darocur 1173	W_2	130	DW
W_2 -DAR-3	70	Darocur 1173	W_2	371	IP 0.5%
W_2 -IRG-1	70	Irgacure 819	W_2	8.8	DW
W_2 -IRG-2	70	Irgacure 819	W_2	5.7	DW
W_2 -IRG-3	70	Irgacure 819	W_2	2.9	DW
OW_2 -DARKPS-1	70	Darocur 1173	O	156	IP 0.5%
		KPS RT	W_2	41	
OW_2 -DARKPS-2	70	Darocur 1173	O	156	IP 0.5%
		KPS 50°C	W_2	41	
OW_2 -DARKPS-3	70	Darocur 1173	O	156	IP 0.5%
		KPS 70°C	W_2	41	
W_1 -AAPH-1	60	AAPH	W_1	12	IP 1.3%
W_1 -AAPH-2	60	AAPH	W_1	12	DW
W_1 -AAPH-3	60	AAPH	W_1	12	PVA + Triton
OW_1 -DARAAPH-1	60	Darocur 1173	O	78	IP 1.3%
		AAPH	W_1	12	
OW_1 -DARAAPH-2	60	Darocur 1173	O	78	DW
		AAPH		12	
OW_1 -DARAAPH-3	60	Darocur 1173	O	78	PVA + Triton
		AAPH	W_1	12	

^a Electrolyte concentration in the carrier phase (W_2): IP 0.5%: 0.5 wt% $CaCl_2$, IP 1.3%: 1.3 wt% $CaCl_2$, DW: distilled water, PVA + Triton: PVA 3 wt% + Triton 3 wt%

5.2.3 Synthesis of macroporous beads by “sedimentation polymerisation”

In order to create polymer beads, a 5 mL syringe was filled with approximately 4 mL of emulsion and equipped with a 22G needle (I.D. 0.41 mm) at the end. The tip of the needle was submerged into a 100 mm diameter Petri dish containing 150 mL of different aqueous solutions as secondary aqueous phase (W_2). Using a syringe pump (Ultimus IV, Nordson EFD, Pforzheim, Germany) emulsion volumes of 0.04 mL were dispensed into the aqueous carrier phase at an injection rate of 0.01 mL/s except otherwise stated. Depending on the W_1/O emulsion injected and the carrier phase (W_2) used, the injection volume and dispense rate were adjusted to produce spherical droplets. Depending on the density difference between

the emulsion droplets and the secondary aqueous phase (W_2) used, the droplets formed after injection slowly sedimented to the bottom of the Petri dish or rose (creamed) to the surface and burst (Table 5-2). However, in some cases it was possible to “stick” the droplets to the glass bottom of the Petri dish by touching the glass surface with the needle tip during injection.

Table 5-2. Summary of the W_1/O emulsion templates and secondary aqueous phases (W_2) composition used to produce macroporous beads. The droplet behaviour after injection into the different secondary aqueous phases (W_2), which is driven by the density difference is presented.

Formulation code	Surfactant conc. [%]	Internal phase volume ratio [%]	Emulsion density [kg/m ³]	Carrier phase used ^b (W_2)	Carrier phase (W_2) density [kg/m ³]	Droplet behaviour
O-DAR-1	15	70	1009.3	IP 1.3%	1013.2	stick to Petri dish
O-DAR-2	15	70	1009.3	IP 0.5%	1005.0	sedimented
O-DAR-3	15	70	1009.3	DW	1000.0	sedimented
O-DAR-4	15	70	1009.3	PVA + Triton	1060.0	stick to Petri dish
W_2 -DAR-1	15	70	1008.9	DW	1002.3	sedimented
W_2 -DAR-2	15	70	1008.9	DW	1001.6	sedimented
W_2 -DAR-3	15	70	1008.9	IP 0.5%	1009.2	sedimented
W_2 -IRG-1	15	70	1008.9	DW	1000.6	sedimented
W_2 -IRG-2	15	70	1008.9	DW	1000.1	sedimented
W_2 -IRG-3	15	70	1008.9	DW	1000.1	sedimented
OW ₂ -DARKPS-1	15	70	1009.3	IP 0.5%	1011.5	stick to Petri dish
OW ₂ -DARKPS-2	15	70	1009.3	IP 0.5%	1011.5	stick to Petri dish
OW ₂ -DARKPS-3	15	70	1009.3	IP 0.5%	1011.5	stick to Petri dish
W ₁ -AAPH-1	15	60	1009.5	IP 1.3%	1013.2	stick to Petri dish
W ₁ -AAPH-2	15	60	1009.5	DW	1000.0	sedimented
W ₁ -AAPH-3	15	60	1009.5	PVA + Triton	1060.0	creamed
OW ₁ -DARAAPH-1	15	60	1009.8	IP 1.3%	1013.2	stick to Petri dish
OW ₁ -DARAAPH-2	15	60	1009.8	DW	1000.0	sedimented
OW ₁ -DARAAPH-3	15	60	1009.8	PVA + Triton	1060.0	stick to Petri dish
^a Surfactant concentrations are with respect to monomer phase						
^b Electrolyte concentration in the carrier phase (W_2): IP 0.5%: 0.5 wt.% CaCl ₂ , IP 1.3%: 1.3 wt.% CaCl ₂ , DW: distilled water, PVA + Triton: PVA 3 wt.% + Triton 3 wt.%						

After injection, the Petri dish containing the emulsion droplets was carefully placed under UV light in order to polymerise the emulsion droplets to produce solid beads. Two different UV light sources were used, namely a UVC-8 Curing Conveyor System (Dymax Europe GmbH, Wiesbaden, Germany) with a maximum intensity of 800 mW/cm² and a 100 W mercury hand held UV light (UVP Blak-Ray B100AP, 365 nm). The lamp of the UVC-8 Curing Conveyor System

was positioned 180 mm above the surface of the conveyor belt working at 90 % of intensity. The conveyor belt speed was kept constant at 1.1 m/s providing an approximate irradiation time of 1 min per run, each Petri dish was placed in the conveyor belt a minimum of 4 times. In the case of droplets irradiated using the hand held UV light, the lamp was placed 100 mm above the glass bottom of the Petri dish.

In the case of OW₂-DARKPS beads, emulsion droplets were injected into aqueous solutions (W₂) heated to at 20°C, 50°C and 70°C. All beads were produced by injecting emulsion volumes of 0.08 ml at 0.03 ml/s into the carrier phase (W₂). The secondary aqueous phase (W₂) consisted of an aqueous solution containing 0.5 wt.% CaCl₂ and the initiator KPS (41 mmol/L). The same KPS concentration in the dispersed phase of W₁/O emulsion templates was used by Wu et al.²⁹⁶ to produce polyMIPes with a close celled structure. The solution was produced by dissolving the initiator and CaCl₂ in an Erlenmeyer flask with distilled water. Approximately 30 mL of this solution were transferred to a sealed Petri dish and heated on a hot plate stirrer equipped with a temperature controller (IKA RCT basic, IKA Ltd, Oxford, England). The droplets remained in the carrier solution (W₂) for different amounts of time and were later exposed to a 100 W hand held UV lamp (UVP Blak-Ray B100AP, 365 nm) for a period of 10 min to complete polymerisation. The beads produced were collected from the container filled with carrier phase (W₂) and placed overnight in a mixture of ethanol and water (50/50 vol.%) to extract all unreacted chemicals. In order to complete purification, the samples were left overnight in distilled water and vacuum dried at 60°C for 12 h.

5.2.4 Synthesis of macroporous beads by “In suspension” polymerisation

The controlled injection of a W₁/O emulsion template into a reactor containing a secondary aqueous phase (W₂) under stirring is a simple solution to produce individual droplets that after polymerisation will become porous beads. Beads were produced by injecting controlled volumes of 0.04 mL of emulsion at a constant injection rate of 0.01 mL/s into a 5 L glass beaker (diameter 18 cm) filled with a 0.5 wt.% CaCl₂ solution under continuous stirring (Figure 5-2).



Figure 5-2. Schematic of the setup used for the production of beads by “in suspension” polymerisation.

A co-flow injection is typically used when low values of droplet size dispersity are desired. In this case, a co-flow geometry was obtained by using an L shaped needle (22G, internal diameter 0.41 mm) at the tip of the syringe pointing in the same direction of the fluid movement. The carrier phase was stirred using a PTFE anchor stirrer connected to an overhead stirrer working at 100 rpm (IKA RW20, IKA Ltd, Oxford, England). The hand held UV light was placed touching the walls of the beaker in order to maximise the UV light irradiation. Between 20 and 40 emulsion droplets were injected and exposed to UV light until rigid beads formed (approximately 15 min). After polymerisation, the stirring was stopped and the beads separated and collected from the carrier phase using a polyester mesh.

5.3 Results and discussion

5.3.1 “In suspension” polymerisation - Influence of stirring rate on bead size

To study the influence of stirring rate on bead size and size dispersion, beads were produced by “In suspension” polymerisation of O-DAR emulsion template droplets. The emulsion was injected into the secondary aqueous phase (W_2) using an injection rate of 0.01 mL/s. After the emulsion injection started, a thread of emulsion approximately 25 mm long formed at the needle tip to be later broken down by the flow turbulence into spherical droplets with an approximate diameter between 0.5 and 1.5 mm. In order to reduce the size dispersion of the droplets formed, the injection volume was reduced from 0.04 mL to 0.02 mL forming a shorter thread of emulsion and droplets of a similar size. The droplets produced sometimes agglomerated and merged forming larger droplets. Also, it was noted that during

polymerisation droplets often stuck together forming permanent clusters. The occasional impact of the stirrer with the emulsion droplets, causing some droplet break up, increased the droplet size dispersion as well. After polymerisation finished, beads with different shapes and sizes were recovered. This can be appreciated in Figure 5-3a showing beads with a broad size dispersion. A closer look at the surface of the beads (Figure 5-3b), reveals an open surface in which surface pore throats can be seen clearly. The internal structure of the beads (Figure 5-3c and d) contained a few pores with a size above 200 μm . The broad pore size dispersion suggests a degree of droplet coalescence in the primary emulsion (W_1/O). All beads had and interconnected internal structure.

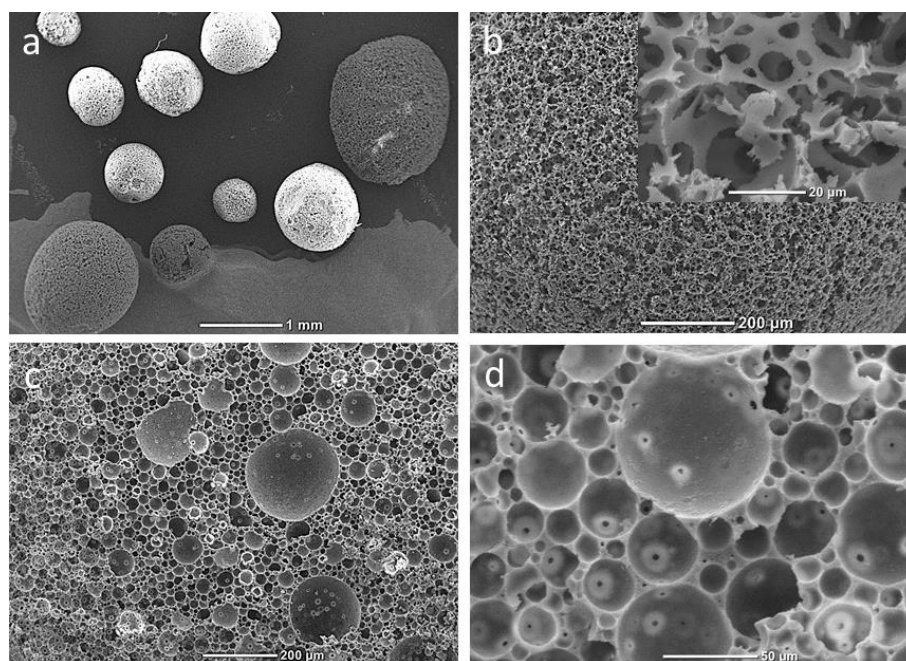


Figure 5-3. SEM images of beads produced by “in suspension” polymerisation of emulsion droplets. The beads produced had a broad size dispersion (a); open surface (b) and interconnected internal pore structure (c and d).

It was observed that the impact of the stirrer with the emulsion droplets had mayor influence on the droplet size dispersion. Further attempts to reduce droplet size dispersion through lower stirring rates (35 and 50 rpm) were performed. In this case, a shorter and ticker emulsion thread formed at the needle tip, leading to larger droplets with a similar diameter. The formed droplets sedimented to the bottom of the beaker staying almost immobile, this reduced the intensity of the UV irradiation, which negatively affected the polymerisation time. The beads recovered were still soft and broke easily even after the irradiation time was increased to 30

min. Unlike beads obtained from stirring at 100 rpm, attachment of emulsion droplets to the glass surface of the beaker after sedimentation was observed, making it difficult to recover the beads.

5.3.2 Determination polymerisation gel point in W_1/O emulsion droplets by “sedimentation polymerisation”

In order to prevent the irreversible agglomeration and deformation of droplets during polymerisation, beads were produced by sedimentation polymerisation of emulsion droplets O-DAR. To determine the minimum amount of time needed to reach the gel point of the polymerisation the emulsion was injected into an aqueous solution of 0.5 wt.% of $CaCl_2 \cdot 2H_2O$ forming spherical droplets. After injection, the emulsion droplets were polymerised using the hand held UV lamp until solid beads were achieved. The advance of polymerisation was followed by carefully squeezing and cutting a few emulsion droplets at regular intervals. The observations made during polymerisation are summarised in Table 5-3.

Table 5-3. Changes in surface structure during polymerisation of droplets from emulsion template O-DAR.

UV Exposition [s]	Changes on droplet surface	Observations
60	A soft shell formed	Droplet deforms under minimum pressure
90	A soft shell formed	Droplet interior is still liquid
120	Sticky gelled like bead formed	Interior of the droplet is gelled
180	Hard surface formed	Breaks easily under pressure
240	The surface was no longer sticky	Idem
300	Idem	Idem
360	Idem	Dramatic increase in resistance
600	Idem	A relatively hard bead is formed

After approximately 5 min of UV light irradiation, the surface of the droplets was not sticky anymore, meaning that if droplets made contact, they did not form permanent agglomerates. After 6 min of irradiation, a dramatic increase in the strength of the droplets was noted and no deformation of the droplets could be observed with the naked eye when squeezed.

5.3.3 Influence of additives to the secondary aqueous phase (W_2) on bead morphology

Beads O-DAR-1 were created by polymerisation of emulsion droplets after injection into a Petri dish containing a 1.3 wt.% CaCl_2 aqueous solution as secondary aqueous phase (W_2). The surface of O-DAR-1 beads (Figure 5-4a) contained circular surface pore throats distributed homogeneously over the surface with an average size of $3.2 \pm 2.3 \mu\text{m}$. Beads O-DAR-2 were created using a CaCl_2 solution with a concentration of 0.5 wt.% as secondary aqueous phase (W_2). The produced beads (Figure 5-4b) possessed smaller but more abundant surface pore throats than previous O-DAR-1 beads with an average size of $1.6 \pm 1.1 \mu\text{m}$. To create O-DAR-3, the procedure was repeated using distilled water as secondary aqueous phase. These beads had surface pore throats with an average size of $4.2 \pm 1.8 \mu\text{m}$ (Figure 5-4c1).

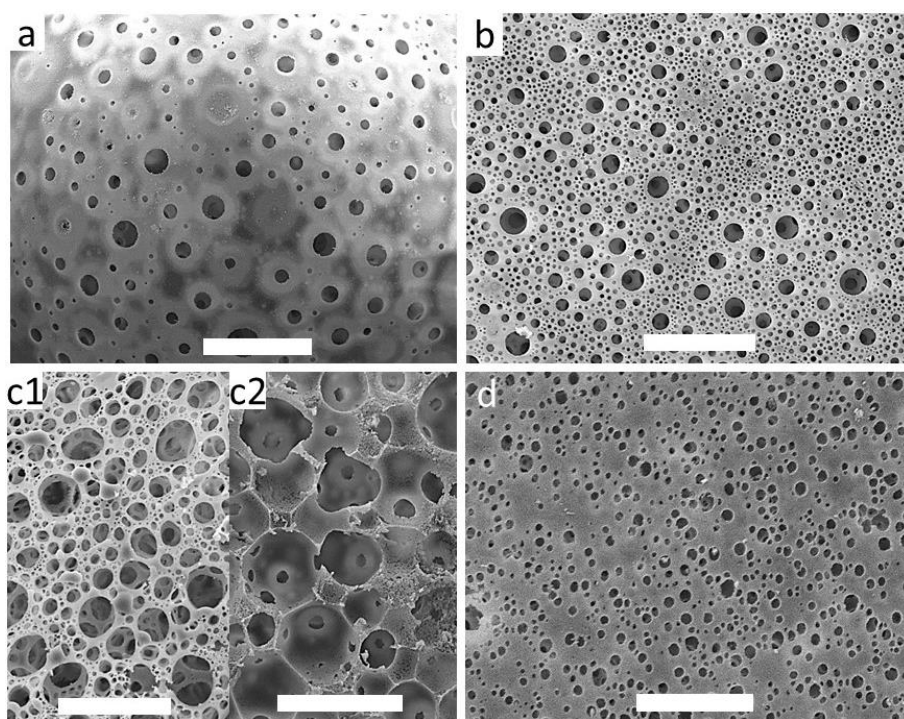


Figure 5-4. SEM images of beads produced by polymerisation of W_1/O emulsion droplets suspended in various secondary aqueous phase (W_2): a) beads O-DAR-1 polymerised in CaCl_2 aq. solution 1.3 wt.%; b) beads O-DAR-2 polymerised in CaCl_2 aq. solution 0.5 wt.%; c1 and c2) beads O-DAR-3 polymerised in distilled water; d) beads O-DAR-4 polymerised in PVA + Triton X-405 aq. solution 3 wt.%. All scale bars represent $50 \mu\text{m}$.

It was observed that the polymer surface of the beads could be eroded easily during sample preparation for SEM, revealing a pore structure with thicker polymer walls and interconnecting pores (Figure 5-4c2). The larger surface pores suggest a superficial

destabilisation of the emulsion before polymerisation. It was also noted that these beads fractured more easily than beads O-DAR-1 and O-DAR-2. As expected, the use of a secondary aqueous phase (W_2) with a lower electrolyte concentration promoted partial destabilisation of the O/ W_2 interface during polymerisation leading to beads with a more open surface. Beads O-DAR-4 were synthesised after emulsion droplets were formed in a secondary aqueous phase containing both, PVA and the surfactant X-405 in a concentration of 3 wt.%. The surface of these beads contained only small surface pore throats ($2.6 \pm 1.1 \mu\text{m}$) homogeneously distributed along the surface (Figure 5-4d).

5.3.4 Production of macroporous beads by “sedimentation polymerisation” of W_1/O emulsion droplets initiated with different photoinitiators in the secondary aqueous phase (W_2)

With the objective in mind to produce beads with an interconnected pore structure but closed surface, the polymerisation of the organic phase of W_1/O emulsion droplets was initiated by using the initiators Darocur 1173 and Irgacure 819 separately in the secondary aqueous phase (W_2). An emulsion was prepared following the steps used previously but without adding initiator to the organic phase. Approximately 30 mL of emulsion were kept inside a sealed centrifuge tube at room temperature in order to study the emulsion stability, after a period 24 h no signs of phase separation were visible.

The first attempt to modify the bead surface was made by using the photoinitiator Darocur 1173 dissolved in the secondary aqueous phase (W_2) with a concentration of 194 mmol/L. The aqueous solution produced was semi-transparent and small droplets of initiator were still visible due to the poor solubility of the initiator in water. After injection, the emulsion droplets flowed nicely from the needle into the secondary aqueous phase forming spherical droplets that sedimented to the bottom of the Petri dish. After the injection was finished, the emulsion droplets were polymerised using the hand held UV light. After 10 min the solution turned whitish and the emulsion droplets were not visible anymore. After 2 h, the UV light was switched off and the carrier phase removed from the Petri dish revealing a set of solid yellowish beads (W_2 -DAR-1). The surface of the beads was not uniform (Figure 5-5a and b), consisting of alternating areas of closed (Figure 5-5c) and open porous areas (Figure 5-5d) with an average surface pore throat size of $3.2 \pm 2.2 \mu\text{m}$.

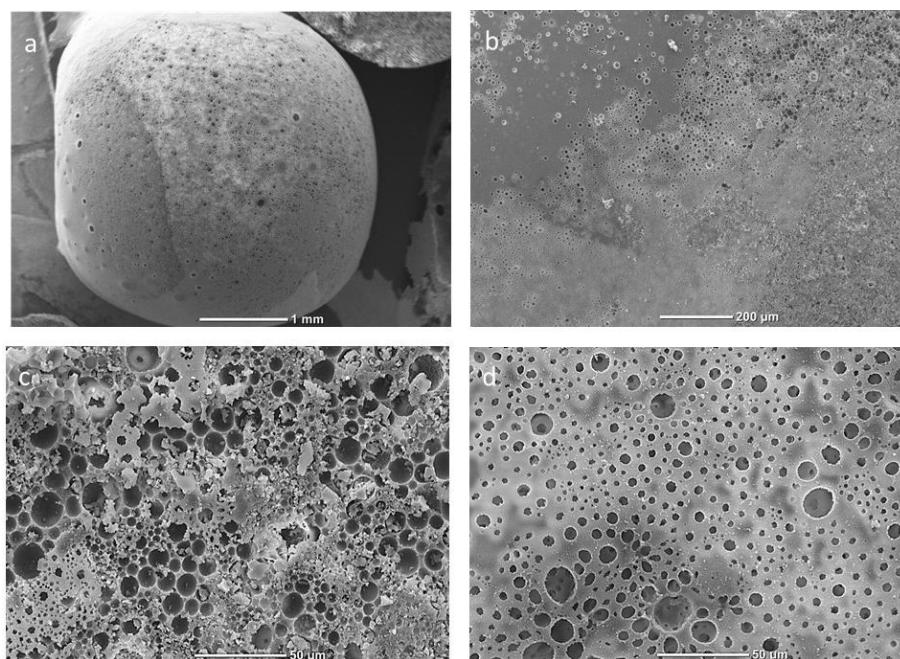


Figure 5-5. SEM images of the surface of W₂-DAR-1 beads, produced by polymerisation using the photoinitiator Darocur 1173 dissolved only in the carrier aqueous phase (W₂).

The internal morphology of the produced beads is shown in Figure 5-6. The presence of a large void in the centre of the bead can be seen in Figure 5-6a, this was a common characteristic in most of the beads produced and was probably caused by partial destabilisation of the emulsion droplets before polymerisation.

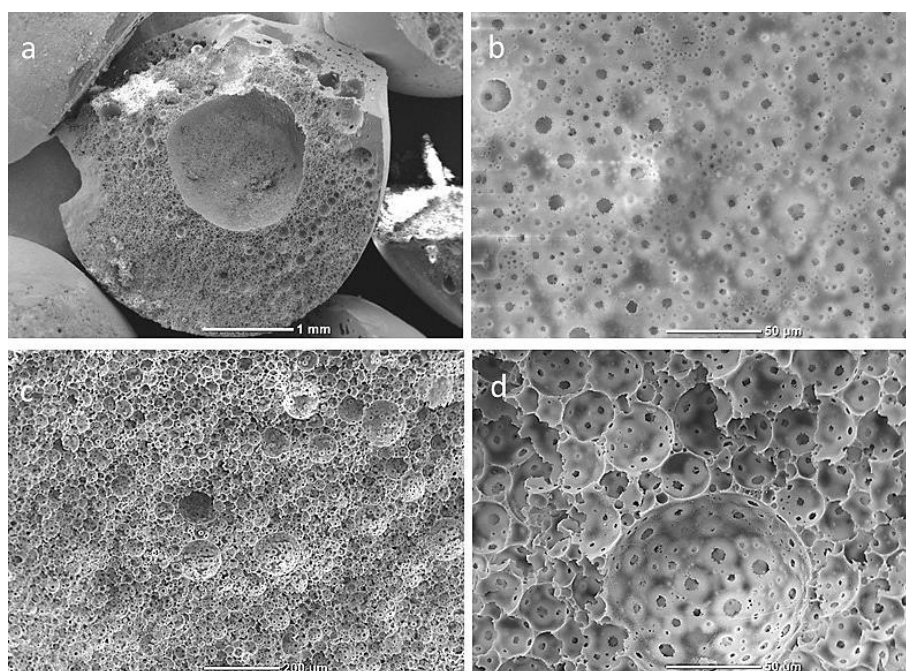


Figure 5-6. SEM images of the internal structure of W₂-DAR-1 beads, revealing an interconnected pore structure with clear signs of emulsion destabilisation.

A closer look revealed the presence of an interconnected pore network not only in the surface of the central void (Figure 5-6b) but in the entire structure of the bead (Figure 5-6c and d). The pore size measured in this case was taken from the rather homogeneous part of the internal pore structure of the beads. For the beads W₂-DAR-1, the average pore size was $18.9 \pm 13.7 \mu\text{m}$ with interconnecting pore throats of $2.7 \pm 1.5 \mu\text{m}$. W₂-DAR-2 beads were produced following the same procedure but reducing the concentration of initiator in the carrier phase (W₂) from 194 to 130 mmol/L. The presence of small initiator droplets in the carrier phase solution after stirring was again observed. After a few minutes of exposure to UV radiation, the semi-transparent phase carrier (W₂) turned whitish and the injected droplets at the bottom of the Petri dish could not be seen anymore. SEM images of the surface and interior of the synthesised W₂-DAR-2 beads were taken. The overall surface of the beads can be seen in Figure 5-7a and b where areas with almost no visible pores (Figure 5-7c) alternate with regions covered with open pores (Figure 5-7d). The morphology of the bead interior pore structure was similar to W₂-DAR-1 beads showing surface pore throats with an average size of $3.8 \pm 3.4 \mu\text{m}$, an increase of almost 20 % with respect to W₂-DAR-1 beads.

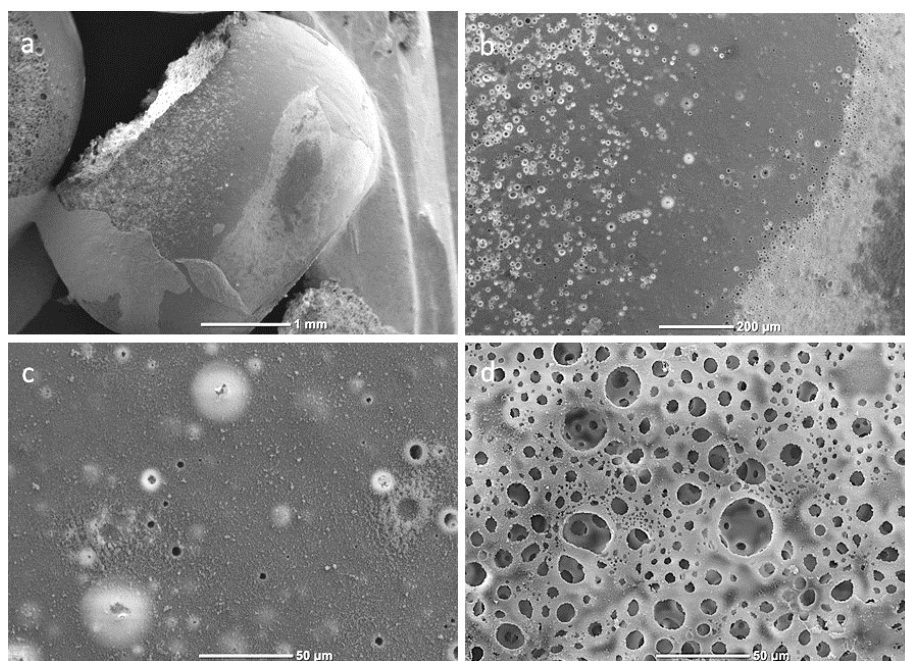


Figure 5-7. SEM images of the surface of W₂-DAR-2 beads. The surface was similar to previous W₂-DAR-1 with slightly larger surface pores.

To analyse the internal morphology of the beads, SEM images from the interior of five fractured beads were taken. All the samples examined contained a big void with an open

porous surface close to the centre of the bead (Figure 5-8a). The rest of the pore structure (Figure 5-8b, c and d) had an average pore size of $18.2 \pm 12.3 \mu\text{m}$, interconnected by pore throats with a size of $2.8 \pm 1.3 \mu\text{m}$, similar to W₂-DAR-1 beads.

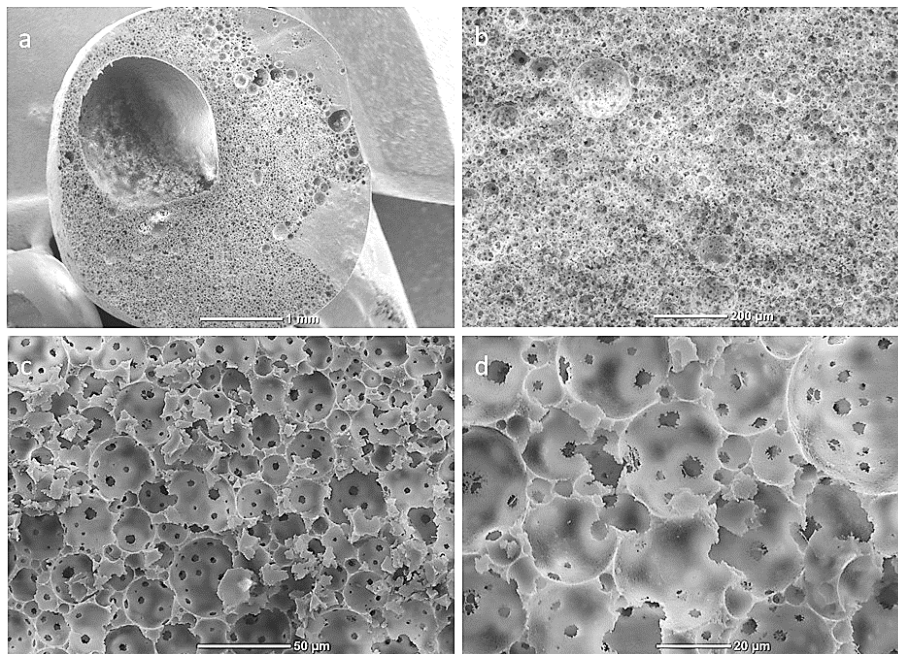


Figure 5-8. SEM images of the internal pore structure of W₂-DAR2 beads. All the samples contained a large void at the centre.

The concentration gradient between the electrolyte used as internal phase (W₁) of the emulsion template (1.3 wt.% CaCl₂) and the secondary aqueous phase W₂ (distilled water) promoted destabilisation of the emulsion droplets causing the formation of the voids in the centre of the beads. However, the surface of W₂-DAR-2 beads showed non-porous areas, indicating moderate success in our attempt to produce beads with a closed surface. Therefore, it was decided to further increase the initiator concentration used in the carrier phase. In an attempt to reduce destabilisation and suppress the formation of voids, the next set of beads was prepared using an aqueous solution of 0.5 wt.% CaCl₂ as secondary aqueous phase (W₂) in which the initiator Darocur 1173 was dissolved until a concentration of 371 mmol/L was reached. After injection, the droplets produced sedimented to the bottom of the Petri dish, where they were polymerised forming W₂-DAR-3 beads. The yield of recovered beads was significantly lower than in previous experiments with approximately only two thirds of the droplets injected recovered as beads. SEM images of the bead surface revealed that areas with open pores were not as frequent as in previous attempts (Figure 5-9a and b). Again,

regions with a predominantly closed surface (Figure 5-9c) alternate with regions containing surface pore throats (Figure 5-9d). Unlike in previous attempts, in areas with surface pore throats, these were isolated and had an average size of $1.4 \pm 0.6 \mu\text{m}$ (Figure 5-9e and f), a reduction of more than 50 % compared with previous W₂-DAR-1 beads. This is likely to be caused by the higher initiator concentration used in the secondary aqueous phase, which resulted in a rapid polymerisation of the O/W₂ interface, reducing the amount and size of the surface pore throats formed.

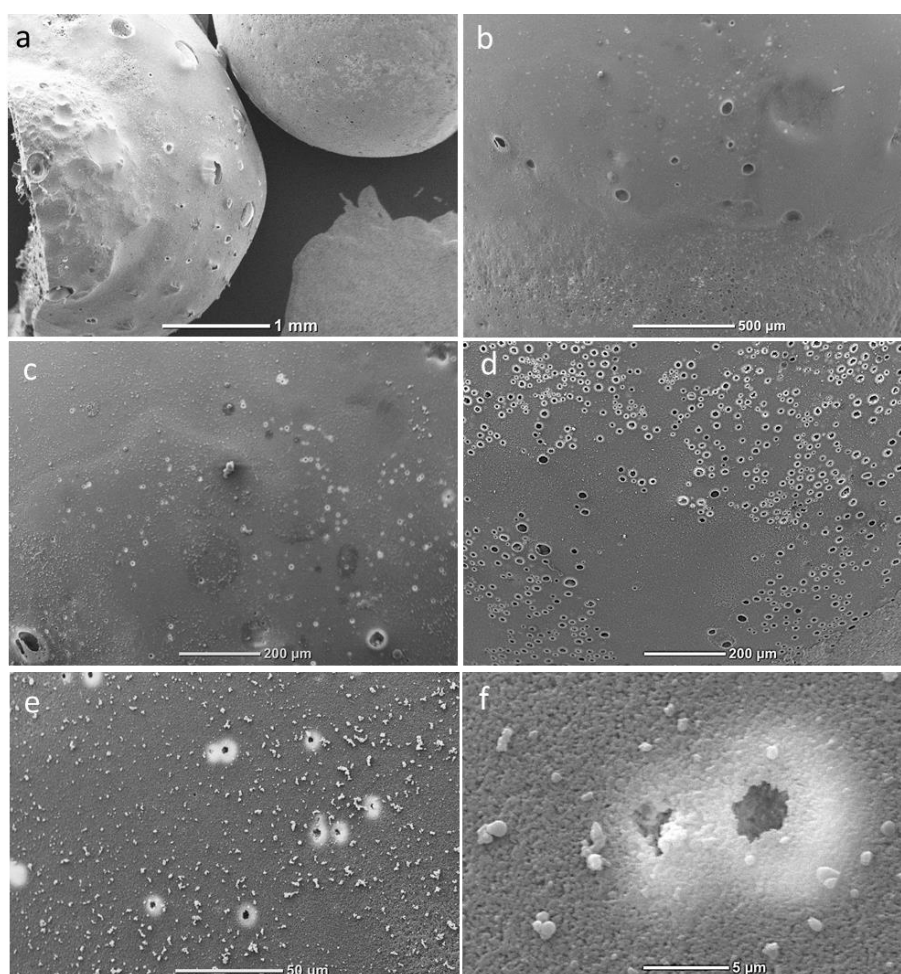


Figure 5-9. SEM images of the surface of W₂-DAR-3 beads. The superficial pores were isolated and smaller compared with W₂-DAR-1 and W₂-DAR-2 beads.

During the preparation of the samples for SEM imaging it was observed that all beads produced contained again a large void in the centre of the beads (Figure 2-10a) likely caused by destabilisation of the emulsion droplets. The internal surface of the void seemed to be covered by a closed skin (Figure 2-10b). The rest of the structure consisted of an interconnected pore morphology with an average pore size of $23.3 \pm 11.1 \mu\text{m}$ and

interconnecting pore throats with a size of $4.3 \pm 1.6 \mu\text{m}$ (Figure 2-10c and d). During sample preparation it was noted that beads were fragile and easily fractured during manipulation, suggesting a mayor destabilisation of the emulsion template during polymerisation. The destabilisation of the emulsion templates (W_2 -DAR), which resulted in a reduced yield and the formation of beads with a large void at the centre could be explained by the longer polymerisation times needed compared with emulsion template droplets where the initiator was dissolved in the organic phase (O-DAR). In this case, even longer polymerisation times were required due to higher absorption of the UV radiation by the carrier phase (W_2) when the initiator concentration was increased. The penetration of UV light was studied during the polymerisation of acrylate layers until a depth of four millimetres.²⁸⁸ The curing kinetics analysed showed that the polymerisation speed decreased due to an increased absorption of UV light caused by a higher initiator concentration in the monomer. In our case, after injection the emulsion droplets slowly settled to the bottom of the Petri dish, which was around 30 mm from the surface of the carrier phase. This distance seemed sufficient to affect the polymerisation time. The natural destabilisation of the emulsion droplets over time resulted in the formation of hollow beads.

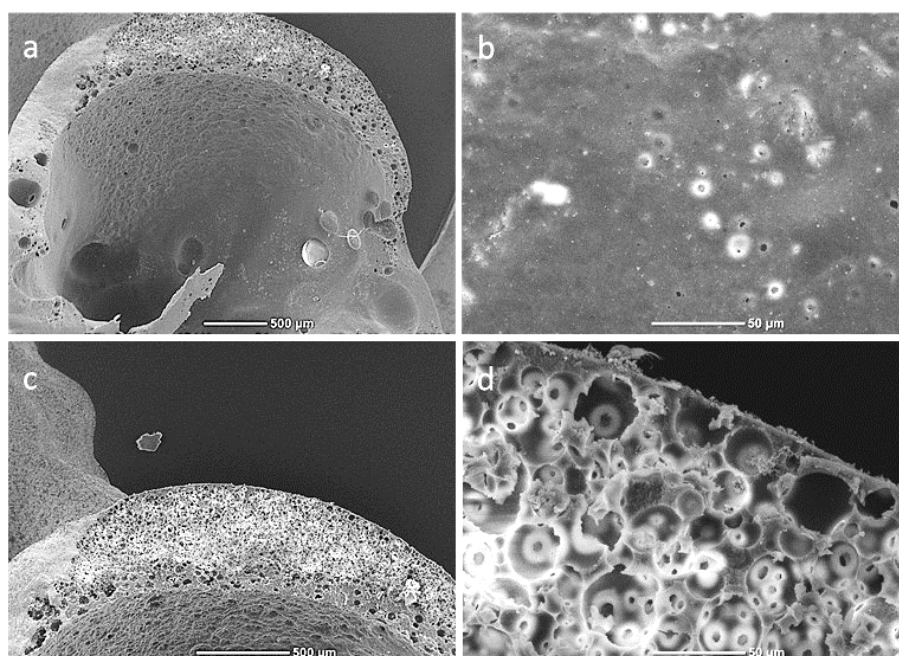


Figure 5-10. SEM images of the internal structure of W_2 -DAR3 beads. A large void formed in the centre of the beads.

In order to reduce the absorption of UV light by the secondary aqueous phase (W_2) and achieve a complete polymerisation of the emulsion droplets, the concentration of photoinitiator dissolved in the secondary aqueous phase (W_2) was reduced. While, the concentration of photoinitiator (Darocure 1173) used in the secondary aqueous phase (W_2) to produce beads W_2 -DAR was 130 mmol/L, beads W_2 -IRG were produced using Irgacure 819 with a concentration below 8.8 mmol/L. The beads produced had a nearly spherical shape with a surface similar to a typical polyHIPE structure with well-defined surface pores and surface pore throats (Figure 5-11a and b). The average size of the surface pores was $22.4 \pm 12.1 \mu\text{m}$ communicating with the bulk pore volume through surface pore throats with an average size of $5.6 \pm 3.2 \mu\text{m}$ (Figure 5-11c and d). The difference in bead surface morphology obtained compared with previous beads W_2 -DAR could be explained by the reduced initiator concentration used in the secondary aqueous phase (from 130 mmol/L to 8.8 mol/L). The lower initiator concentration could lead to a polymerisation of the system from less initiation points, increasing the polymerisation time and the relaxation time, resulting in a typical polyHIPE structure at the bead surface.

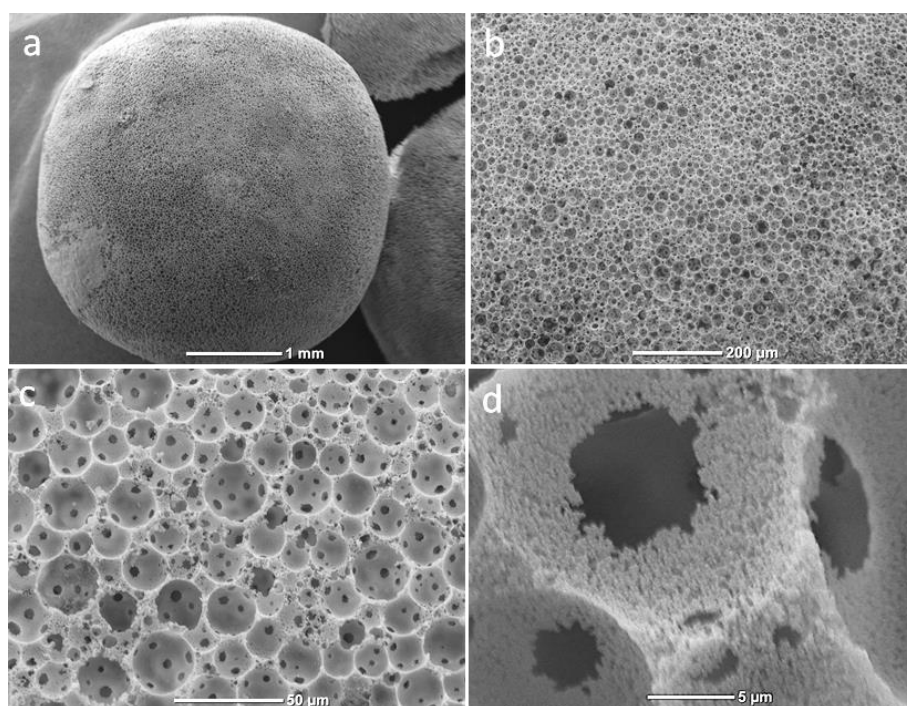


Figure 5-11. SEM images of the surface of W_2 -IRG-1 beads.

Analysis of the internal morphology of W_2 -IRG-1 beads revealed a rather homogeneous interconnected pore structure (Figure 5-12a and b) consisting of pores with an average size of

$20.9 \pm 11.8 \mu\text{m}$ and interconnecting pore throats of $3.6 \pm 1.6 \mu\text{m}$ (Figure 5-12c and d). The average pore throat size of W₂-IRG-1 beads compared with the surface pore throat size was more than 35 % smaller. No signs of emulsion destabilisation could be observed after polymerisation in the interior of the beads. It is worth mentioning that during sample preparation for SEM imaging, W₂-IRG-1 beads did not break as easily as W₂-DAR-3 beads, however, they were friable and eroded easily by friction with other beads during storage.

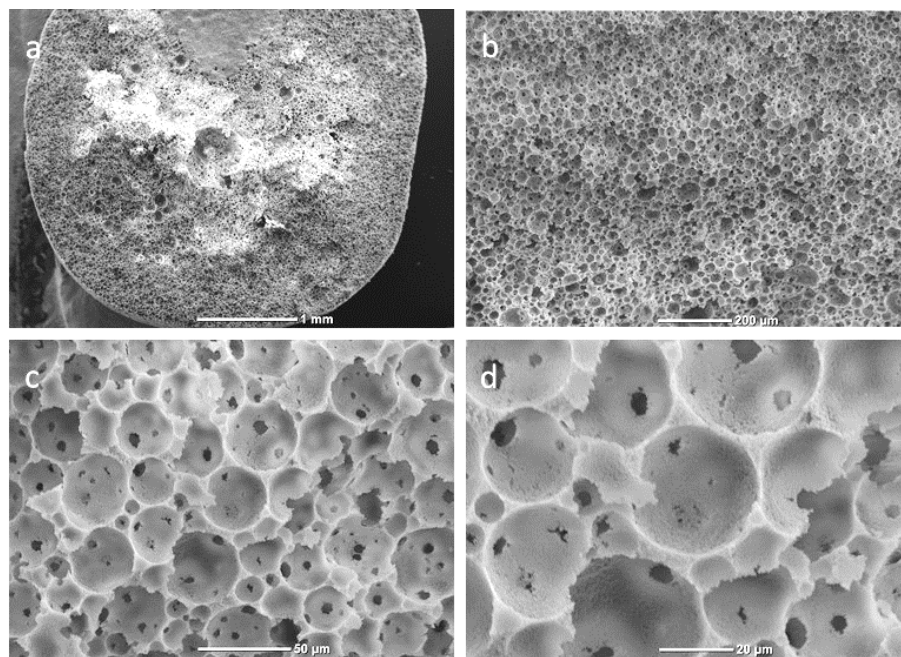


Figure 5-12. SEM images of the internal pore structure of W₂-IRG-1 beads.

To produce W₂-IRG-2 beads, the same emulsion was injected into a secondary aqueous phase (W₂) containing an aqueous solution with a reduced Irgacure 819 concentration (from 8.8 to 5.7 mmol/L). A cloudy secondary aqueous phase (W₂) was formed after the initiator was stirred to form the solution. After injecting the emulsion into the secondary aqueous phase (W₂), spherical droplets formed and sedimented to the bottom of the Petri dish. After polymerisation for 20 min, white beads with an approximate diameter of 2 mm (Figure 5-13a) were recovered. An SEM image of the beads surface can be seen in Figure 5-13b and c revealing a homogeneous porous structure similar to W₂-IRG-1 beads. In this case, the average size of the surface pore throats was $4.4 \pm 1.7 \mu\text{m}$ (Figure 5-13d), presenting a reduction of more than 20 % compared with the superficial pores of W₂-IRG-1 beads ($5.6 \pm 3.2 \mu\text{m}$).

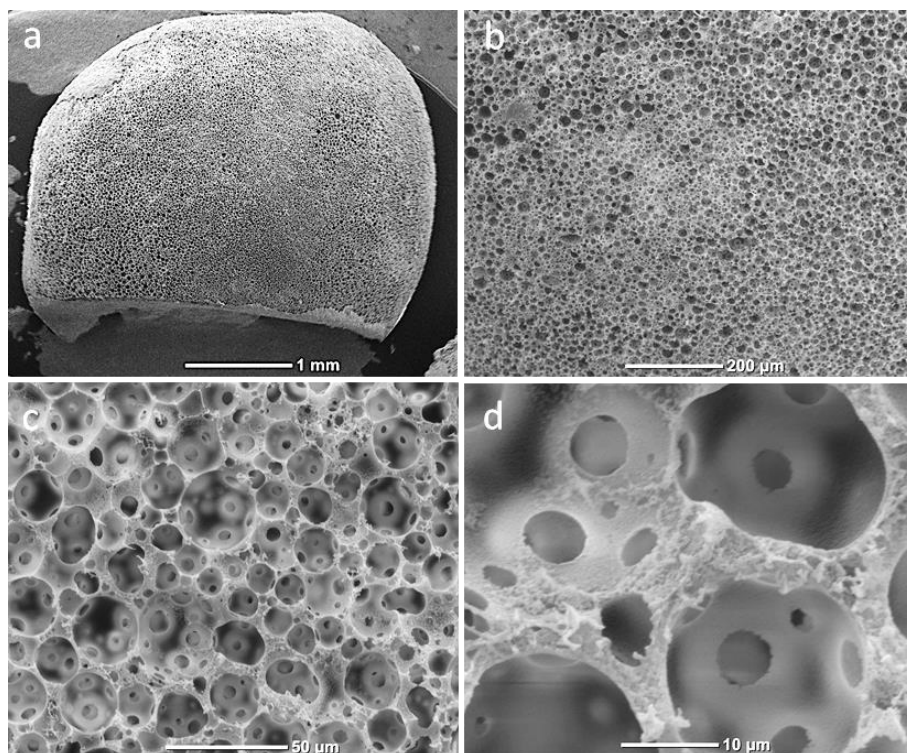


Figure 5-13. SEM images of the surface of W₂-IRG-2 beads, having a homogeneous open porous surface.

When preparing samples for SEM imaging, it was noticed that more than approximately 2/3 of the beads contained a large void inside (Figure 5-14a). SEM images of the internal pore structure of the beads revealed an interconnected pore network (Figure 5-14c and d) with an average pore size of $18.2 \pm 12.3 \mu\text{m}$.

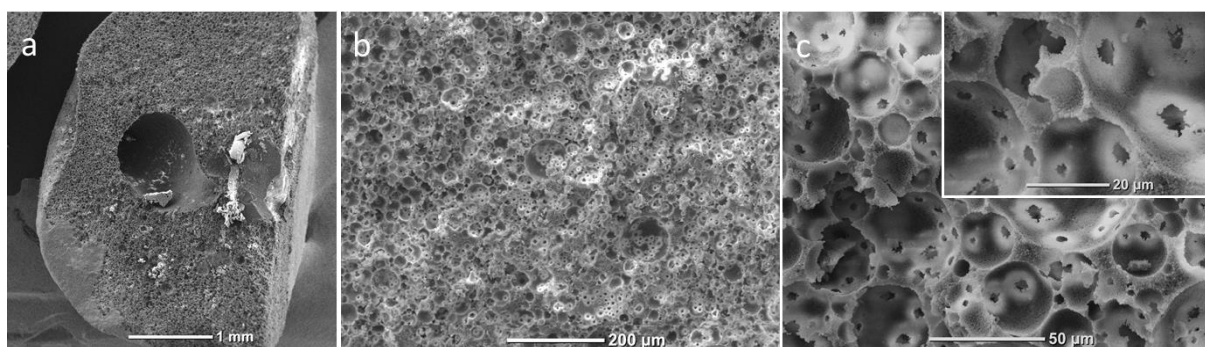


Figure 5-14. SEM images of the internal pore structure of W₂-IRG-2 beads. a) A large void with a diameter of approximately 1 mm in size in the centre was observed in approximately 2/3 of the beads. An interconnected pore structure was present in all beads produced.

The interconnecting pore throats had an average size of $2.8 \pm 1.1 \mu\text{m}$, which corresponds to a reduction of 20 % compared with W₂-IRG-1 beads. It is worth mentioning that the relative

pore throat size, defined as the ratio between pore throat size and pore size (Equation 3-8) for beads W₂-IRG-1 and W₂-IRG-2 was similar in both cases, with a value of 17 and 15 %, respectively. As before, the interconnecting pore throats at the surface of the beads were more than 35 % bigger than pore throats in the interior of beads. This difference could be explained by the partial destabilisation of the O/W₂ interface due to a delayed polymerisation compared with W₂-DAR beads, produced in a secondary aqueous phase (W₂) with higher initiator concentrations. To produce W₂-IRG-3 beads the initiator concentration in the secondary aqueous phase (W₂) was further reduced from 5.7 to 2.9 mmol/L. The surface of the beads produced was homogeneous but open porous (Figure 5-15a and b).

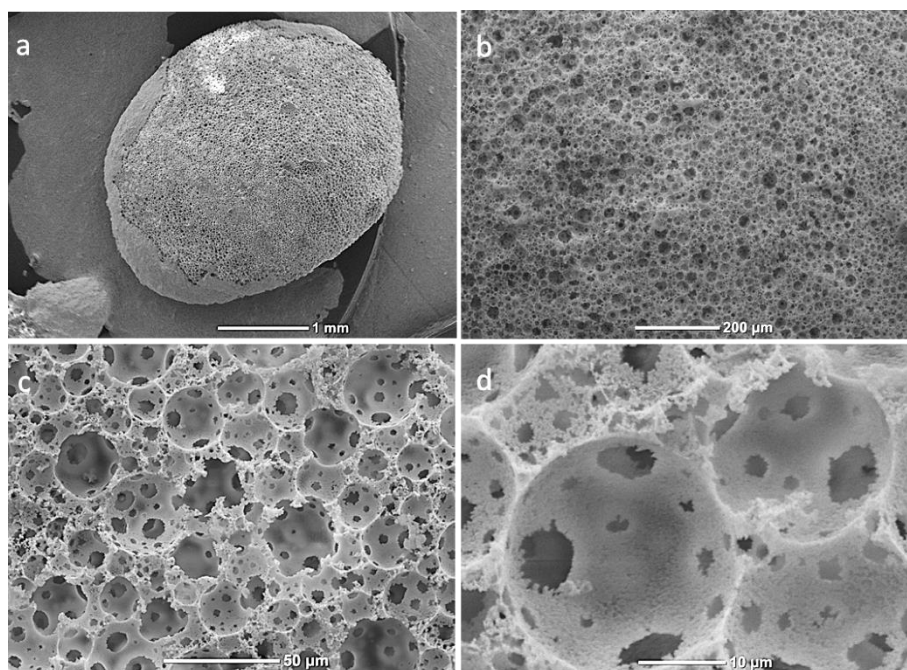


Figure 5-15. SEM images of the surface of W₂-IRG-3 beads. The beads produced had a homogeneous surface with interconnecting surface pore throats.

A closer look at the bead surface revealed an interconnected porous structure with an average pore size of $15.7 \pm 8.4 \mu\text{m}$ (Figure 5-15c). The surface pore throats had an average size of $3.2 \pm 1.3 \mu\text{m}$ (Figure 5-15d), a reduction of almost 30 % compared to W₂-IRG-2 beads and of more than 40 % to W₂-IRG-1 beads. An analysis of the internal structure of beads W₂-IRG-3 revealed a homogeneous pore size distribution except in approximately 1/3 of the beads. These beads had a small void in the centre (Figure 5-16a); a result of emulsion destabilisation during polymerisation. The pore structure resembled W₂-IRG-1 beads and had an average pore size of $19.3 \pm 11.7 \mu\text{m}$ (Figure 5-16b and c). The average pore throat size was $2.9 \pm 1.4 \mu\text{m}$, a

reduction of 20 % compared with the initial beads W₂-IRG-1 (Figure 5-16d) but the relative pore throat size remained constant (15 %). When surface and internal pore throats were compared, only a small difference of 10% was observed (from $3.2 \pm 1.9 \mu\text{m}$ for the surface pore throats to $2.9 \pm 1.4 \mu\text{m}$). In the case of W₂-IRG-1 and W₂-IRG-2, which had larger surface pore throats, this difference was 56 % and 57 %, respectively.

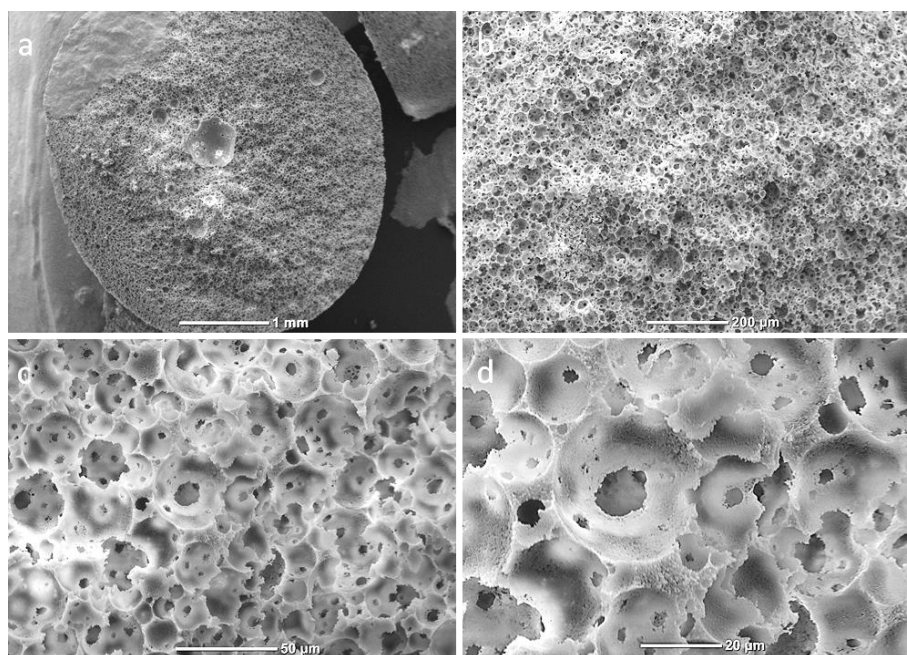


Figure 5-16. SEM images of the internal structure of W₂-IRG-3 beads. a) A small fraction of the beads produced (approximately 1/3) had a void in the centre; b), c) and d) All beads produced had an interconnected pore structure.

The reduction in surface pore throat size and relative pore throat size observed in W₂-IRG-3 beads produced with lower concentrations of photoinitiator in the secondary aqueous phase (W₂) could, as in the transition from W₂-DAR beads to W₂-IRG beads, be explained by the lower initiator concentration in the secondary aqueous phase. During polymerisation, the continuous phase at the O/W₂ interface shrinks, a lower initiator concentration reduces the polymerisation initiation points, resulting in a slower polymerisation. The slower polymerisation allows the formation of a typical polyHIPE structure at the bead surface containing surface pore throats instead of a closed surface.

5.3.5 Production of macroporous beads by polymerisation of W_1/O emulsion template droplets using initiator in the organic phase (O) and secondary carrier phase (W_2)

In an attempt to produce beads with a close celled surface but an interconnected pore morphology in the interior, initiators were dissolved in both the organic phase of the W_1/O emulsion and in the secondary aqueous phase (W_2). The primary emulsion droplets were injected into the secondary aqueous phase (W_2) leading to beads (OW₂-DARKPS) after polymerisation (Figure 5-17).

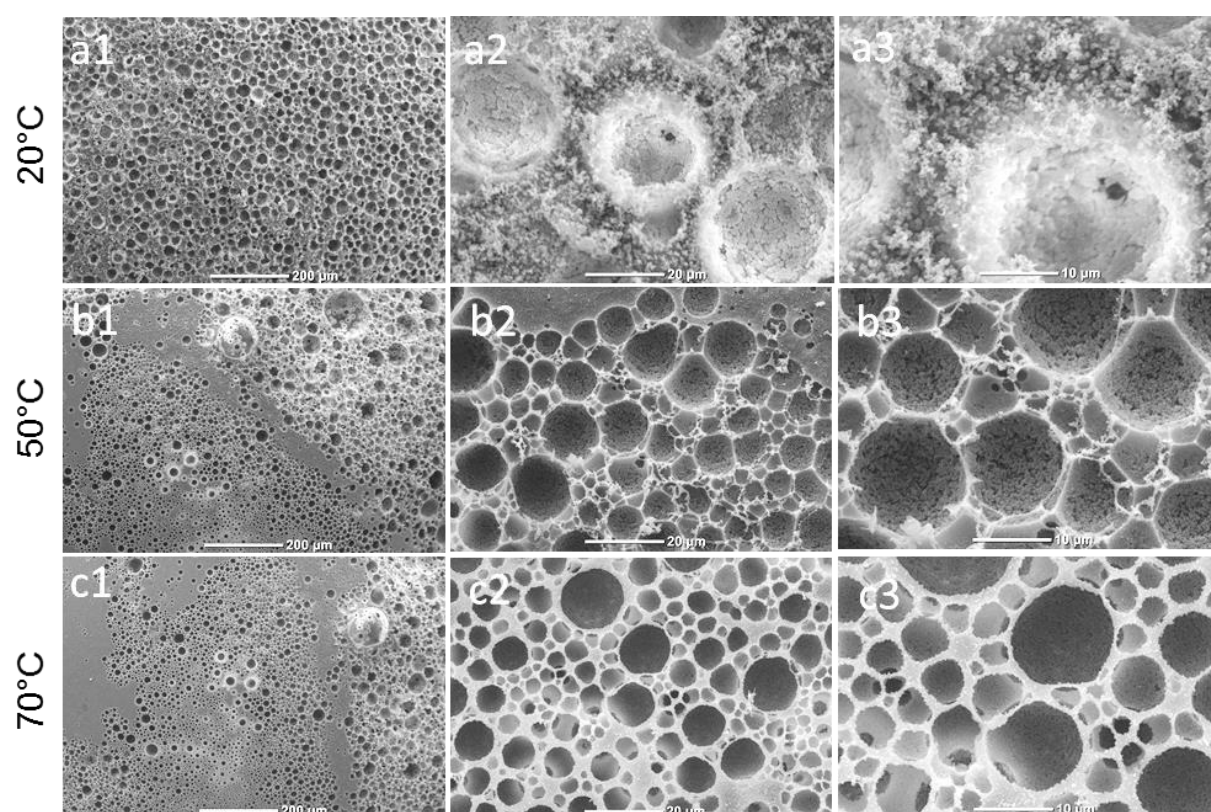


Figure 5-17. SEM images of macroporous beads produced by polymerisation of emulsion droplets suspended in a secondary aqueous carrier phase (W_2) at different temperatures. a) OW₂-DARKPS-1 beads, polymerised at 20°C; b) OW₂-DARKPS-2 beads, polymerised at 50°C and c) OW₂-DARKPS-3 beads, polymerised at 70°C.

The first set of beads (OW₂-DARKPS-1) was produced by injecting the emulsion into an aqueous solution (W_2) containing 0.5 wt.% CaCl₂ and the initiator KPS with a concentration of 41 mmol/L at room temperature ($\sim 20^\circ\text{C}$). When preparing OW₂-DARKPS-1 beads, it was noted that a few seconds after injection the formed droplets rose to the surface due to the lower density of the W_1/O emulsion (Table 5-2) and disintegrated. In order to keep the droplets submerged in the aqueous solution, the W_1/O emulsion droplets were “attached” to the glass

surface. After injection, the droplets possessed a semi-spherical shape (approximately 80 % of the volume of an entire sphere). The deformed droplets remained in the carrier solution for 1 h and were later exposed to UV light for a period of 10 min. The surface of beads polymerised at 20 °C (Figure 5-17a) was homogeneous, containing surface pores with an average size of $22.6 \pm 7.7 \mu\text{m}$ and a few surface pore throats with an average size of $2.2 \pm 1.9 \mu\text{m}$ (Figure 5-17 a3). In the case of OW₂-DARKPS-2 beads, produced after injection into a carrier phase (W₂) at 50 °C, “sticking” the emulsion droplets to the surface of the Petri dish was more difficult as only minor vibrations caused a large amount of droplets to detach from the glass surface, cream and disintegrate at the solution (W₂) surface. The droplets were kept inside the warm carrier phase (W₂) for a period of 15 min and then carefully exposed to UV light for 10 min. A decrease in droplet size was noted when the droplets remained inside the carrier phase (W₂) for longer periods of time without being exposed to UV light. This size reduction could be due to destabilisation of the emulsion at higher temperatures. The solid beads recovered after polymerisation possessed a surface with smooth areas and no visible pores and areas with a morphology similar to OW₂-DARKPS-1 beads with closed pores containing only a few surface pore throats (Figure 5-17 b1). The interconnecting pore throats had an average size of $2.8 \pm 1.1 \mu\text{m}$ (Figure 5-17 b2 and b3). When the temperature of the solution was raised to 70 °C (OW₂-DARKPS-3), keeping the droplets attached to the bottom of the Petri dish after injection was almost impossible and droplets had to be exposed to UV light immediately after injection in order to avoid their disintegration. The surface of the beads (Figure 5-17 c1) was similar that of previous OW₂-DARKPS-2 beads. In these beads the presence of areas with pore throats was more common showing a similarity to beads produced when the initiator was only present in the organic phase of the emulsion (beads O-DAR). The internal pore structure of OW₂-DARKPS-1 beads (Figure 5-18 a1) had a narrow pore size distribution, despite being in the secondary aqueous phase (W₂) for 1 h, no significant evidence of phase separation was observed after polymerisation of the emulsion template (Figure 5-18 a2 and a3). In case of OW₂-DARKPS-2 and OW₂-DARKPS-3 beads, a few pores with an approximate size of 300 μm were observed (Figure 5-18 b1 and c1), indicating the onset of phase separation in the emulsion template prior to polymerisation. This is represented by the standard deviation of the average pore size, with values higher than the average pore size for both OW₂-DARKPS-2 ($26.4 \pm 52.6 \mu\text{m}$) and OW₂-DARKPS-3 beads ($23.2 \pm 44.9 \mu\text{m}$). Partial destabilisation of the emulsion templates can be explained by the increase in temperature of the secondary

aqueous phase (W_2), promoting droplet coalescence in the (W_1/O) primary emulsion, which resulted in an increasingly broader pore size distribution after polymerization.

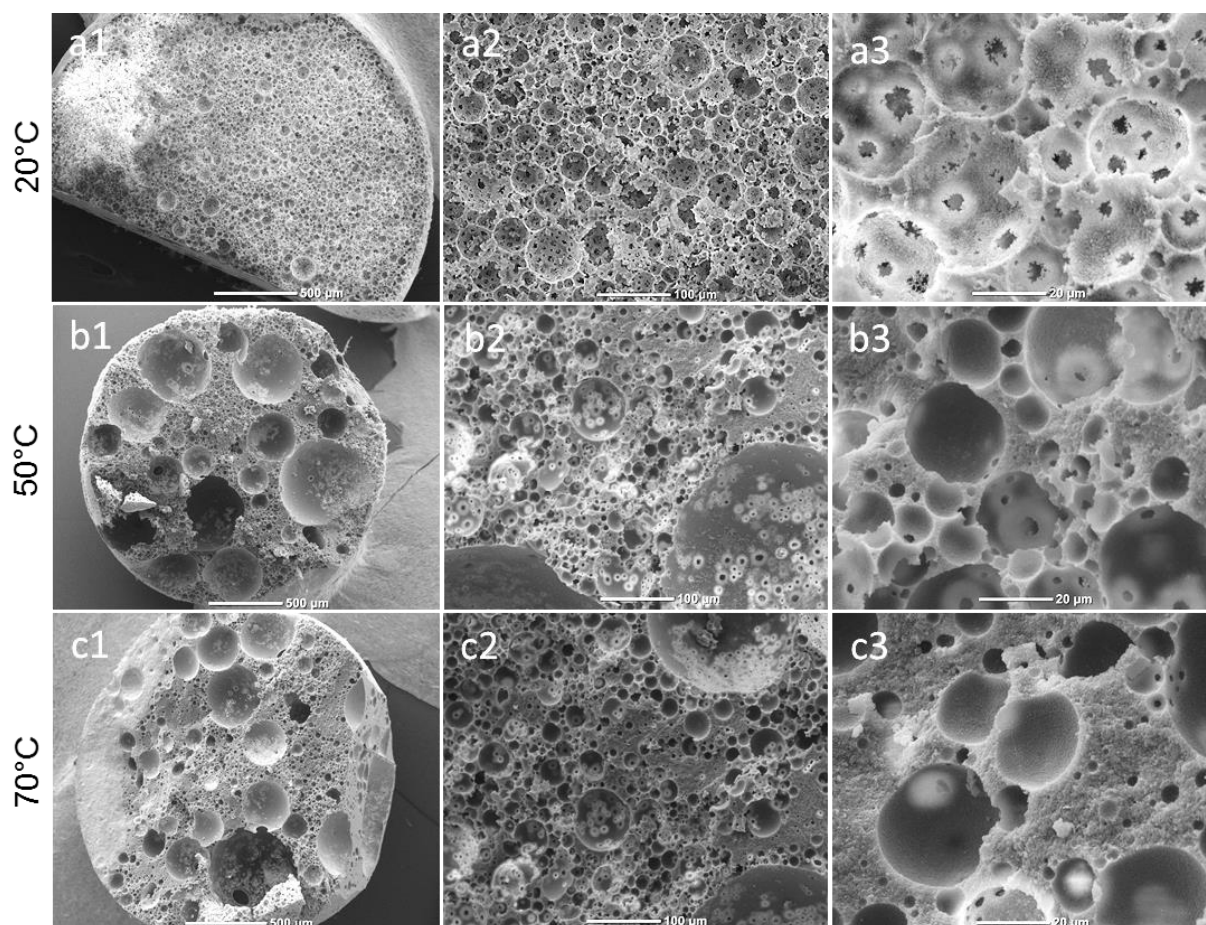


Figure 5-18. SEM images of the internal structure of beads produced by polymerisation of emulsion droplets in a carrier phase (W_2) at different temperatures. a) OW_2 -DARKPS-1 beads, polymerised at 20 °C; b) OW_2 -DARKPS-2 beads, polymerised at 50 °C and c) OW_2 -DARKPS-3 beads, polymerised at 70 °C.

It can be observed that for beads created by injection in a carrier phase at room temperature (OW_2 -DARKPS-1), the use of KPS promoted the formation of beads with a close surface. However, the combination of higher temperatures needed to initiate the thermal polymerisation and the longer polymerisation times required were detrimental for the stability of the (W_1/O) primary emulsion.

5.3.6 Production of macroporous beads by polymerisation of W_1/O emulsion template droplets using initiator in the dispersed aqueous phase of the emulsion (W_1)

In order to avoid premature destabilisation of the emulsion template droplets after injection into the secondary aqueous phase (W_2), the use of UV light to generate free radicals needed to initiate the polymerisation was preferred over thermally initiated polymerisation. A different approach was used by dissolving a photoinitiator in the aqueous dispersed phase of the emulsion (W_1). The initiator chosen was the water soluble photoinitiator 2,2'-azobis(2-methylpropionamidine) dihydrochloride (AAPH). This initiator was successfully used by Lyoo et al.³¹⁰ at a concentration of 3.7 mmol/L as replacement for KPS for the emulsion polymerisation of vinyl acetate. While AAPH and KPS react under thermal dissociation (at working temperatures between 50 °C and 70 °C), AAPH can also decompose to form radicals when exposed to UV radiation. After injection into an aqueous solution (W_2) containing 1.3 wt.% $CaCl_2$, the emulsion droplets ($\rho \sim 1010 \text{ kg/m}^3$) creamed and disintegrated at the surface of the secondary aqueous phase (W_2), which had a density of $\sim 1013 \text{ kg/m}^3$. Therefore, in order to keep the droplets submerged in the aqueous solution, their surfaces were attached to the glass bottom of the Petri dish. After irradiation with a hand held UV lamp for a period of 30 min, the emulsion droplets could be easily deformed by contact with a spatula. To achieve polymerisation, the UVC-8 Curing Conveyor System was used with the conveyor belt running at 1.1 m/s providing an irradiation time to the droplets of approximately 45 s per run. After 3 min, the droplets had a jelly-like surface, showing a partial success in the curing. However, after 8 min of irradiation a slight increase in the temperature of the carrier phase (W_2) due to the heat released by the UV lamp was noted. In order to prevent destabilization, the polymerisation continued using the hand held UV lamp. After 2 h, polymerisation was terminated by switching off the UV lamp and the produced W_1 -AAPH-1 beads were washed and dried. The surface of the beads produced was covered by wrinkles (Figure 5-19a and b) and no pores or surface pore throats could be observed (Figure 5-19c). The internal structure of the beads was rather homogeneous, with closed celled pores of irregular shape (Figure 5-19e and f) with an average pore size of $4.1 \pm 1.9 \text{ }\mu\text{m}$ (equivalent to circular pores). The use of a photoinitiator in the dispersed phase of the emulsion templates (W_1) promoted the formation of a polymer skin around the water droplets during polymerisation, which prevented the formation of interconnecting pore throats.

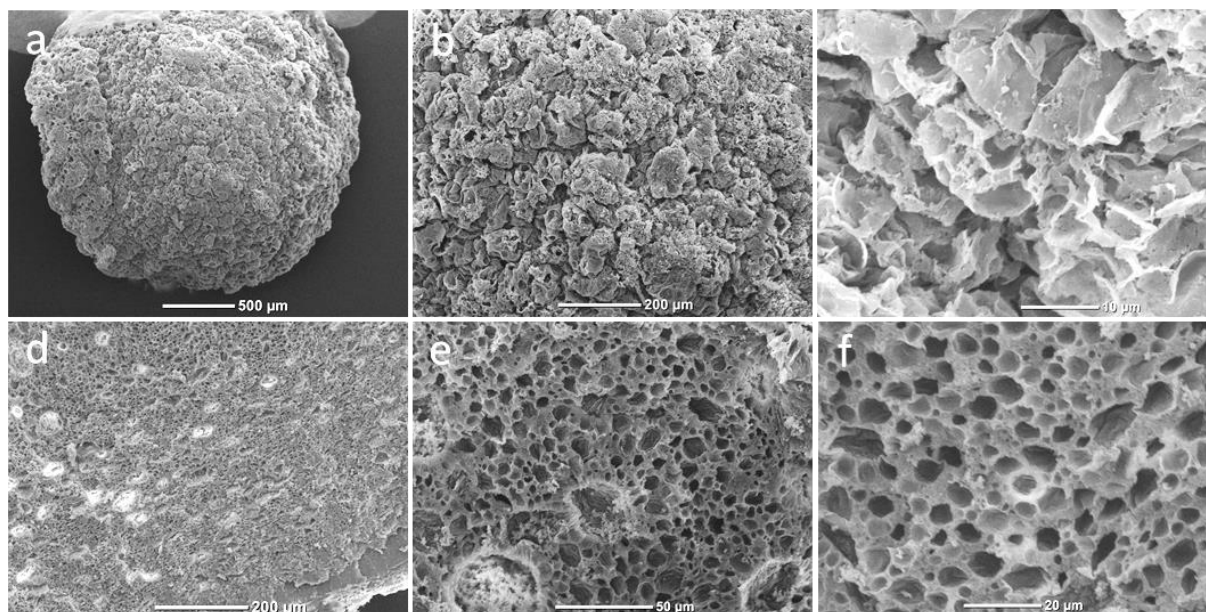


Figure 5-19. SEM images of W_1 -AAPH-1 beads; images a), b) and c) show the bead surface while images d), e) and f) show the closed celled internal pore structure of the beads.

The non-circular shape of the pores might be formed due to shrinkage of the polymer layer around the water droplets and at the bead surface due to the density increase during the transformation of monomer into polymer, causing also the formation of surface wrinkles (Figure 5-19c). The shrinkage of MIPEs in which the polymerisation is initiated at the W_1/O interphase was observed by Wu et al.²⁹⁶, they suggested that could be caused by residual surfactant acting as plasticiser that could not be removed during purification due to the closed cell structure of the samples. Beads W_1 -AAPH-1 were mechanically weak, with a friable structure that could be destroyed easily when squeezed, which can also be attributed to the plasticising effect of the surfactant. In monoliths produced by polymerisation of emulsion templates with the same emulsion formulation in the UVC-8 Curing Conveyor System, shrinking was observed before purification and drying of the samples (Figure 2-20a and b). In this case, the monoliths could be easily fractured by hand.

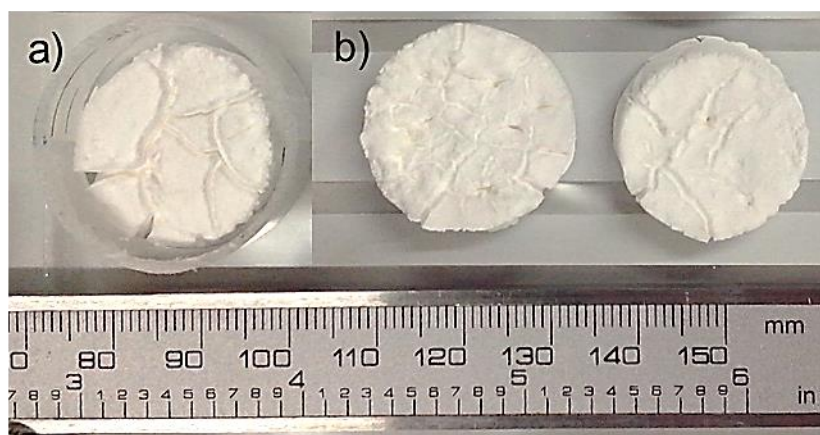


Figure 5-20. Monoliths produced by polymerisation of emulsion templates initiated from the dispersed phase (W_1): a) before demoulding and b) after demoulding

The same experiment was repeated using two different secondary carrier phases, distilled water and a 3 wt.% solution of PVA and Triton X-405. After injection of the emulsion into distilled water, the droplets sedimented to the bottom of the Petri dish due to the density difference between the emulsion ($\sim 1009 \text{ kg/cm}^3$) and the distilled water. After approximately 9 min under the UVC-8 Curing Conveyor System, only a soft shell was formed on the droplet surface. As before, to complete the polymerisation the Petri dish with the droplets was placed under the hand held UV light for a period of 2 h. However, after that period of time, only rests of polymer could be recovered possibly due to destabilisation of the emulsion in the distilled water. When the experiment was repeated injecting the emulsion into a 3 wt.% solution of PVA and Triton X-405 ($\rho = 1060 \text{ kg/m}^3$) all droplets produced creamed and disintegrated at the air/water surface of the solution due to the density differences between the emulsion and the secondary aqueous phase. Similar results were obtained when different injection volumes and injection speeds were used.

5.3.7 Production of macroporous beads by polymerisation of W_1/O emulsion template droplets using initiator in the dispersed aqueous phase (W_1) and organic phase (O) of the emulsion templates

In order to improve the strength of the beads produced, polymerisation was not only initiated in the dispersed phase of the emulsion (W_1) but also simultaneously in the organic phase (O) using the photoinitiator Darocure 1184 leading to OW_1 -DARAAPH beads. The formulation and emulsification conditions used to produce the emulsion templates W_1 -AAPH were repeated

but the photoinitiator Darocur 1173 was added to the organic phase of the emulsion in a concentration of 78 mmol/L. After stirring, a stable white emulsion with $\rho = 1010 \text{ kg/m}^3$ and milky viscosity was obtained. Beads OW₁-DARAAPH-1 were synthesised by injecting emulsion volumes of 0.02 mL at 0.003 mL/s into an aqueous solution of CaCl₂ with a concentration of 1.3 wt.%, the same electrolyte used as internal phase of the emulsion. Spherical droplets formed, again creamed to the air/water surface of the carrier phase and disintegrated. To keep the emulsion droplets in the solution, the droplets were attached to the Petri dish surface, creating non-spherical droplets. After the injection was completed, the Petri dish containing the droplets was run through the UVC-8 Curing Conveyor System two times (approximately 2 min of UV exposure) in order to polymerise the monomer phase. The semi-solid beads obtained were placed under the hand held UV light for 2 h to complete polymerisation, resulting in white spherical beads with a small flat side after purification. Beads OW₁-DARAAPH-2 were produced by injecting the emulsion into distilled water using the same injection and polymerisation conditions. In this case due to the lower density of distilled water, all formed droplets sedimented to the bottom of the Petri dish. Beads OW₁-DARAAPH-3 were obtained after emulsion was injected into an aqueous solution containing 3 wt.% of PVA and Triton X-405. Previous injection conditions were repeated but due to the higher density of the carrier phase used ($\rho = 1060 \text{ kg/m}^3$), it was almost impossible to keep the formed droplets attached to the bottom of the Petri dish. Therefore, only 3 beads could be produced. In an attempt to keep the droplets in the aqueous solution, several volumes and injection speeds were tested leading to similar results. The surface of OW₁-DARAAPH-1 beads (Figure 5-21a) was partially open with surface pore throats with an average size of $1.9 \pm 1.0 \text{ }\mu\text{m}$ and zones with a smooth closed surface (Figure 5-21 a3).

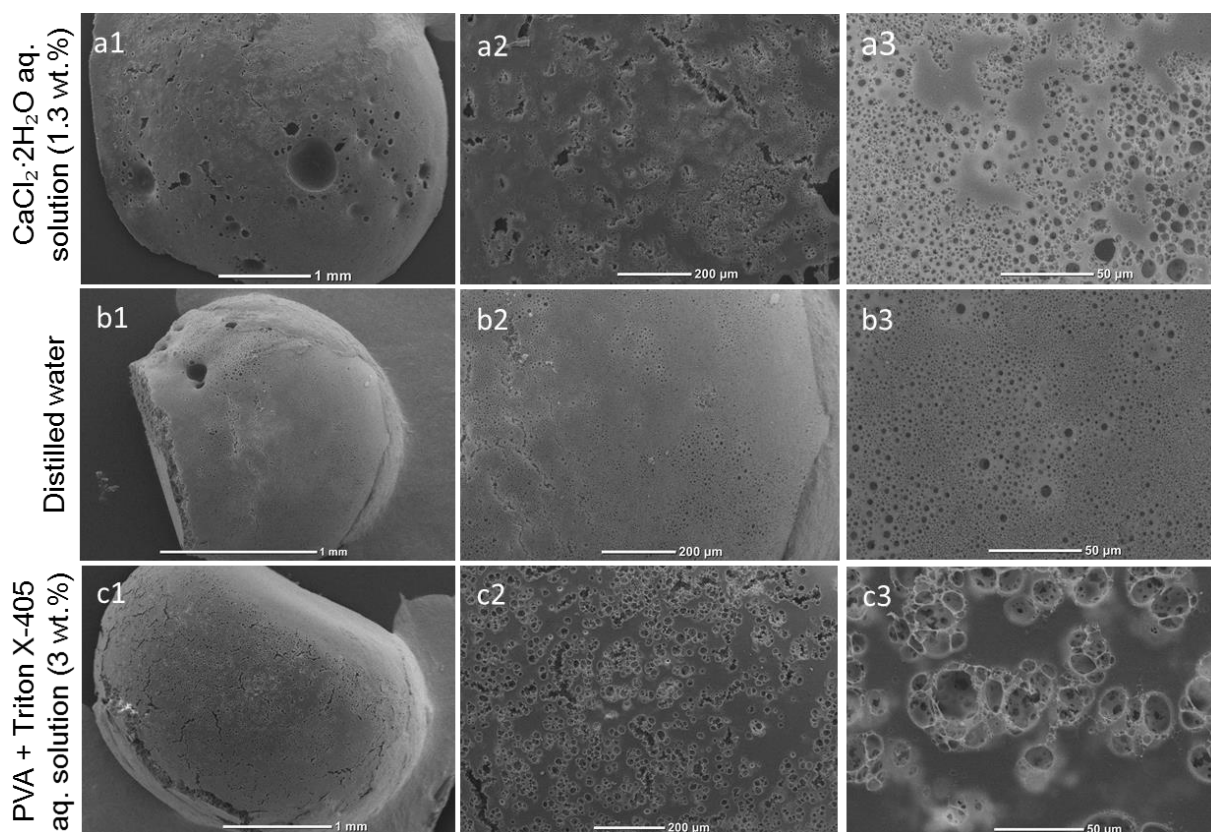


Figure 5-21. SEM images of the surface of OW₁-DARAAPH beads after injection and polymerization in different secondary aqueous phases (W₂), a) CaCl₂·2H₂O aq. solution 1.3 wt.%; b) Distilled water and, c) 3 wt.% aqueous solution of PVA and Triton X-405.

Beads produced from emulsion droplets injected into distilled water (OW₁-DARAAPH-2) showed a surface with homogeneously distributed surface pore throats (Figure 5-21b and c) with an average size of $0.9 \pm 0.5 \mu\text{m}$. The surface had pore throats of the same magnitude of beads O-DAR-3, produced after injection of emulsion templates containing the photoinitiator Darocur 1173 in their organic phase into distilled water. When the emulsion was injected into PVA/Triton X-405 solution, the surface of the beads produced (OW₁-DARAAPH-3) resemble the beads OW₁-DARAAPH-1 combining a surface with closed areas and surface pore throats with an average size of $1.7 \pm 1.1 \mu\text{m}$. However, in OW₁-DARAAPH-3 beads, fewer surface pores were observed. It appears to be that the presence of the hydrophilic surfactant Triton X-405 in the secondary aqueous phase (W₂) stimulated the formation areas with a closed surface. The internal structure of beads OW₁-DARAAPH can be seen in Figure 5-22. All beads produced using this emulsion template possessed spherical pores instead of the rounded but irregular pore shapes obtained when emulsions containing only the initiator AAPH in the internal phase were used (W₁-AAPH beads).

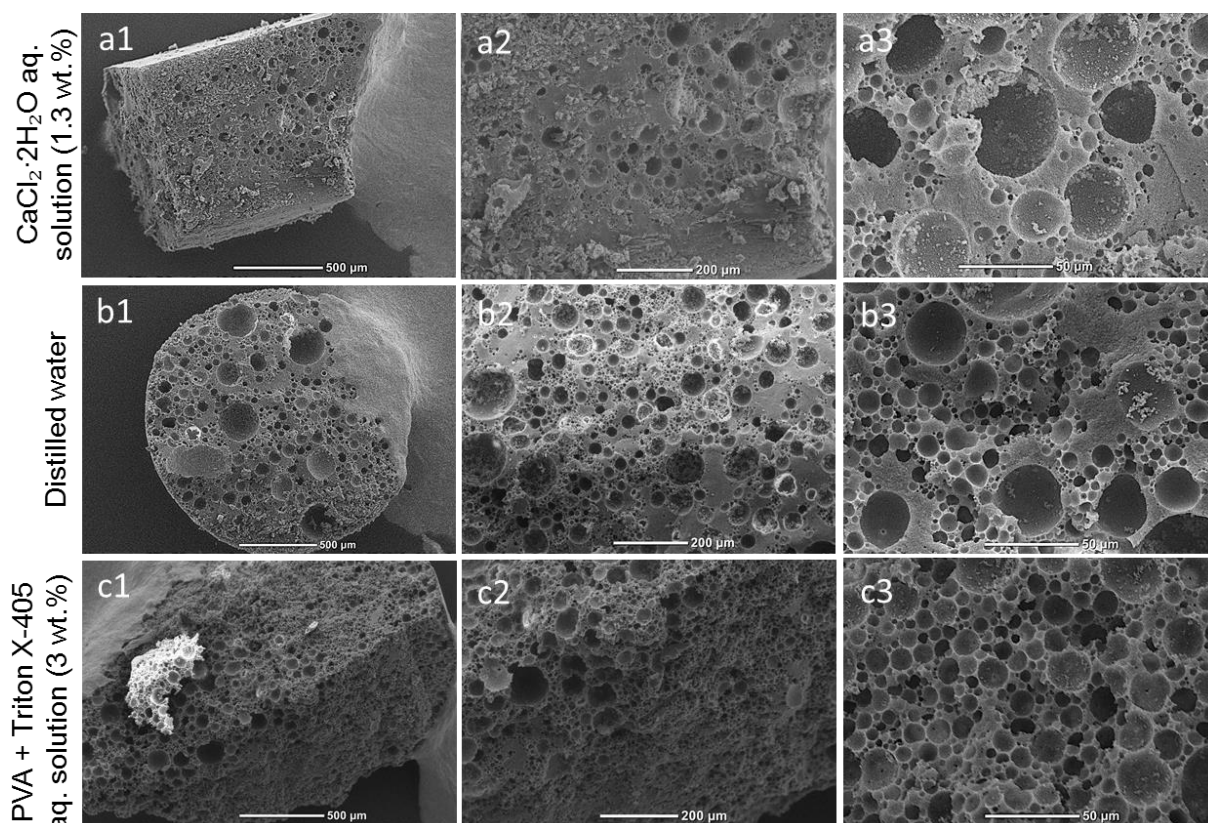


Figure 5-22. SEM images of the internal structure of OW₁-DARAAPH beads after injection and polymerization in different secondary aqueous phases (W_2), a) $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ aq. solution 1.3 wt.%; b) Distilled water and, c) 3 wt.% aqueous solution of PVA and Triton X-405.

It is worth mentioning that porous beads obtained using this formulation were mainly close celled, compared with the previously synthesised O-DAR beads with initiator only in the organic phase, which had an interconnected internal pore structure. This characteristic can be attributed to the influence of initiation from the internal interface (W_1/O). A summary of all the average pore, pore throat and surface pore throat sizes of the beads produced is presented in Table 5-4.

Table 5-4. Summary of the internal and surface pore size and pore throat size of macroporous beads produced by polymerisation of emulsion templates used in this chapter.

Formulation code	Internal phase volume ratio [%]	Location of the initiator ($W_1/O/W_2$)	Carrier Phase (W_2) used ^a	Pore size [μm]	Pore throat size [μm]	Relative pore throat size ^b [%]	Surface pore size [μm]
O-DAR-1	70	O	IP 1.3%	17.1 ± 10.4	2.7 ± 1.2	16%	3.2 ± 2.3
O-DAR-2	70	O	IP 0.5%	17.0 ± 15.5	2.9 ± 1.0	17%	4.2 ± 1.8
O-DAR-3	70	O	DW	11.3 ± 10.5	2.8 ± 1.3	25%	1.6 ± 1.1
O-DAR-4	70	O	PVA + Triton	16.3 ± 9.5	3.4 ± 1.4	21%	2.6 ± 1.1
W_2 -DAR-1	70	W_2	DW	18.9 ± 13.7	2.7 ± 1.5	14%	3.2 ± 2.2
W_2 -DAR-2	70	W_2	DW	18.2 ± 12.3	2.8 ± 1.3	15%	3.8 ± 3.4
W_2 -DAR-3	70	W_2	IP 0.5%	23.3 ± 11.1	4.3 ± 1.6	18%	1.4 ± 0.6
W_2 -IRG-1	70	W_2	DW	20.9 ± 11.8	3.6 ± 1.6	17%	5.6 ± 3.2
W_2 -IRG-2	70	W_2	DW	18.2 ± 12.3	2.8 ± 1.1	15%	4.4 ± 1.7
W_2 -IRG-3	70	W_2	DW	19.3 ± 11.7	2.9 ± 1.4	15%	3.2 ± 1.3
OW_2 -DARKPS-1	70	O- W_2	IP 0.5%	21.2 ± 14.0	2.1 ± 1.3	10%	2.2 ± 1.9
OW_2 -DARKPS-2	70	O- W_2	IP 0.5%	26.4 ± 52.6	2.8 ± 1.0	11%	2.8 ± 1.1
OW_2 -DARKPS-3	70	O- W_2	IP 0.5%	23.2 ± 44.9	2.5 ± 1.0	11%	2.9 ± 1.1
W_1 -AAPH1	60	W_1	IP 1.3%	4.1 ± 1.9^b	Closed pores	N/A	Closed pores
W_1 -AAPH2	60	W_1	DW	No beads	No beads	N/A	No beads
W_1 -AAPH3	60	W_1	PVA + Triton	No beads	No beads	5%	No beads
OW_1 -DARAAPH-1	60	W_1 -O	IP 1.3%	11.6 ± 12.7	Closed pores	N/A	1.9 ± 1.0
OW_1 -DARAAPH-2	60	W_1 -O	DW	15.4 ± 18.7	Closed pores	N/A	0.9 ± 0.5
OW_1 -DARAAPH-3	60	W_1 -O	PVA + Triton	7.3 ± 5.7	0.4 ± 0.1	5%	1.7 ± 1.1

^a Electrolyte concentration in the carrier phase: IP 0.5%: 0.5 wt.% CaCl_2 , IP 1.3%: 1.3 wt.% CaCl_2 , DW: distilled water, PVA + Triton: PVA 3 wt% + Triton 3 wt%

^b Equivalent diameter (non-spherical pores)

5.4 Summary

The surface interconnectivity with the internal pore network of macroporous beads produced by polymerisation of multiple emulsion templates ($W_1/O/W_2$) was controlled by modifying the composition of the secondary aqueous carrier phase (W_2) and locus of initiation of polymerisation, i.e. from W_1 , W_2 , O or combinations thereof. The use of an appropriate combination of hydrophilic surfactants in the secondary aqueous phase (W_2), in this case PVA and Triton X-405, led to beads (O-DAR-4) with fewer and smaller surface pores, thus reducing interconnectivity. A significant reduction in the size (50 %) but not in the amount of pore throats creating interconnectivity with the bulk pore network was observed when the droplets of emulsion template were polymerised in distilled water (O-DAR-3 beads) instead of calcium chloride electrolyte.

Additionally, macroporous beads were produced by using different initiators in the secondary aqueous phase (W_2). The concentration of the initiators used (Darocur 1173 and Irgacure 819) influenced the pore throat size and, therefore, connectivity of the external bead surface. In beads created using Irgacure as initiator (W_2 -IRG), only pore throats connected the surface with the interior of beads. In this case lower initiator concentrations resulted in smaller pore throat sizes on the bead surface. For W_2 -DAR beads, produced using Darocur 1173 as photoinitiator in the secondary aqueous phase (W_2), a reduction in the average size of surface pore throats of 56 % was achieved after the initiator concentration was increased from 130 to 371 mmol/L. These beads had a surface consisting of alternating non-porous regions and zones containing surface pore throats.

The injection of W_1/O emulsion templates containing the photoinitiator Darocur 1173 dissolved in the organic phase into a secondary aqueous phase (W_2) containing the water soluble initiator KPS was less successful. In this case, a heated secondary aqueous phase above room temperature to increase the initiator decomposition rate caused the emulsion to destabilise. However, at room temperature a reduction in the average size and occurrence of superficial pore throats was observed.

Beads with a close celled surface and a closed internal morphology (W_1 /AAPH beads) were produced when using the water soluble photoinitiator AAPH dissolved in the dispersed phase of the emulsion templates (W_1) and reducing the internal phase volume ratio from 70 to 60 %. However, the beads produced were fragile. In order to improve the mechanical strength of the beads, the photoinitiator Darocur 1173 was used in the organic phase of the emulsion (OW_1 -DARAAPH beads). The beads produced after polymerisation in a $CaCl_2$ electrolyte (W_2) were difficult to break when squeezed with a pair of tweezers and had a surface consisting of closed areas and zones containing surface pore throats. Similar results were observed after injection and polymerisation of the emulsion templates into a solution containing PVA and Triton X-405. In this case, beads with surface pore throats of $1.7 \pm 1.1 \mu m$ were produced. The internal structure of these beads was interconnected with pore throats of $0.4 \pm 0.1 \mu m$, the smallest of all formulations tested.

Chapter 6. Micro vs. macrofluidics. Who wins? A new approach to scale up production of macroporous particles

6.1 Introduction

Macroporous beads containing an encapsulated active ingredient are attractive for several applications, such as delivery systems for additives down well or self-healing agents in composites.¹⁴ The trigger for the release of the encapsulated active ingredients may vary depending on the intended application, for example, it can be released by crushing the beads or through progressive degradation of the polymer walls by chemical or mechanical means. Unlike capsules, in which fracture of the shell causes a complete release of the encapsulated ingredient, the pore structure of macroporous beads determines the release rate of the encapsulated active ingredient. In the case of beads with highly interconnected pore structures, a complete and fast release is more likely to occur. However, if the beads have a close celled pore morphology the active ingredient will be released only from the fractured pores. Another advantage of macroporous beads compared with capsules is that the remaining structure is still capable of bearing some load after fracture. This feature is especially attractive for application as delivery vehicle of healing agents in composite materials. The pore morphology of macroporous beads produced by polymerisation of multiple emulsion templates can be tailored by controlling the composition of the emulsion templates used^{32, 158} and the emulsification parameters.¹⁴³ The synthesis of macroporous beads by polymerisation of suitable multiple emulsion ($W_1/O/W_2$) templates by suspension or sedimentation polymerisation has several restrictions that limit its use above lab scale; Beads produced by suspension polymerisation^{168, 215} have a broad size dispersion which requires separation to obtain beads with the desired size range and therefore a reduced yield. On the other hand, beads produced by sedimentation polymerisation¹⁵⁴ are typically monodisperse with a size dispersion below 5 % but high production rates are difficult to obtain due to the buoyancy forces acting on the droplets after release. Moreover, bead size can only be accurately controlled by changing the needle diameter. Moreover, suspension and sedimentation polymerisation are not continuous processes, and therefore, controlling the bead size or modifying the composition of the emulsion templates used require time

consuming preparations. The more recent development of microfluidic UV polymerisation allowed for the production of beads with very narrow size dispersion and the possibility to tailor bead size by controlling the flow rates used.^{199, 248} Bead size and size dispersion are controlled by the droplet breakup of the emulsion during injection of the emulsion into the carrier phase. Depending on the flow ratios between the injected emulsion and the carrier phase, droplet breakup occurs in the dripping or jetting regime. If the droplet breakup takes place in the laminar dripping regime, the droplets are formed at the needle tip and tend to be spherical with a low size dispersion (compared with particles produced in the jetting regime).²²⁹ In contrast, if droplet breakup occurs in the jetting regime, an unstable thread of emulsion is formed at the tip of the needle. This thread, also known as jet or finger will break up into droplets with different sizes. The transition from an emulsion thread or jet into individual droplets begins with the development of small perturbations, known as Rayleigh instabilities,²²⁴ on the surface of the emulsion injected. The tendency to form a thread or jet is influenced by carrier phase velocity, injection velocity, emulsion viscosity and the interfacial tension between the emulsion continuous phase and carrier phase. The interfacial tension between the two fluids causes the formation of spherical droplets and is the only force that opposes the generation of a jet.³¹¹ Additionally, the droplet size is influenced by the viscosity of the carrier phase, the injector needle and channel diameters.²¹⁹ As presented in Chapter 2, a common setup used for the production of droplets with a controlled size dispersion is the co-flow geometry.²⁴⁶ In this case the emulsion is injected in the direction of the flowing carrier phase. The production rate of emulsion droplets that after polymerisation of the continuous organic phase form macroporous beads in co-flow geometries is controlled by the injection flow rate of the emulsion into the carrier phase, which is one of the main drawbacks of microfluidic devices. If the emulsion injection flow rate is increased to raise the production rate while the carrier phase flow rate is kept constant, the droplet size generally increases.³⁴ This may be undesired in certain applications and often causes clogging of the device.²⁴⁸ If the carrier phase flow rate is further increased to maintain a desired droplet size, besides a higher consumption of carrier phase, the exposure of the droplets to UV irradiation is reduced, which can lead to an incomplete polymerisation. Thus, frequent clogging of the setup and the low production rates are two important limitations encountered when producing macroporous polymer beads in microfluidics devices.

In this chapter we introduce a new approach for the production of macroporous beads by polymerisation of multiple emulsion templates in macrofluidic plug flow reactors. In our process, emulsion template droplets with a controlled size and size dispersion are produced in a co-flow geometry by varying the injection and carrier phase flow rates. After polymerisation, the produced beads can be easily collected and separated without the need to stop the process, leading not only to larger production volumes but avoiding clogging of the reactor. Additionally, W_1/O emulsion templates containing hydrochloric acid in the dispersed phase of the emulsion were injected and polymerised into a recirculating carrier phase (W_2) to test the encapsulation potential of beads produced in our macrofluidic device.

6.2 Experimental

6.2.1 Materials

The monomer methyl methacrylate (MMA), crosslinker ethylene glycol dimethacrylate (EGDMA), calcium chloride dihydrate ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$), the emulsifiers polyvinyl alcohol (PVA) with an average molecular weight of 30.000-70.000 g/mol, poly(ethylene glycol)-block-poly(propylene glycol)-block-poly(ethylene glycol) MW = 2800 g/mol (Pluronic L-81) and octylphenol ethoxylate (Triton X-405), sodium hydroxide (>98 %), hydrochloric acid solution (37 vol.%) and the indicator phenolphthalein were purchased from Sigma-Aldrich (Vienna, Austria). The photoinitiator 2-hydroxy-2-methyl-1-phenyl-1-propanone (Darocur 1173) was kindly donated by BTC Europe GmbH (Düsseldorf, Germany). All chemicals were used as received.

6.2.2 Preparation of emulsion templates

In order to prepare stable emulsion templates, the surfactant Pluronic L-81, used previously to formulate M/HIPEs with a relatively low viscosity, was used in different concentrations with respect to the organic phase. The photoinitiator Darocur 1173 was dissolved in the organic phase of the emulsion (O) in order to initiate polymerisation after exposure to UV light. The dispersed phase of the emulsion templates (W_1) used in this chapter consisted of an aqueous solution containing 1.3 wt.% (13.2 g/L) of $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ as an electrolyte in order to suppress Ostwald ripening. The emulsion templates were prepared by mixing the continuous yet minority organic phase in a reactor vessel (glass, 250 mL volume) fitted with a glass paddle

rod (2 blades, anchor shape) connected to an overhead stirrer (Heidolph RZR 2102 Control, Heidolph Instruments GmbH, Schwabach, Germany) for 5 min at 500 rpm. Afterwards, the dispersed aqueous phase was added dropwise into the reactor while keeping the stirring speed constant. Following the addition of the dispersed aqueous phase, stirring continued for another 10 min at 500 rpm to obtain a homogeneous emulsion. The rheological behaviour of the emulsion templates tested was described in Chapter 4, it was observed that the emulsion templates became increasingly viscous with increasing internal phase volume ratio and surfactant concentrations. In order to distinguish beads produced in the macrofluidic plug flow reactor from beads produced by sedimentation polymerisation, the prefix “Mac” replaced the letter “E” in the nomenclature. For example, beads produced by polymerisation of the emulsion templates E15-50, which were stabilised using a surfactant concentration of 15 vol.% with an internal phase volume ratio of 50 % were named Mac15-50. Additionally, emulsion templates containing different amounts of HCl as model active ingredient were prepared by replacing one third of the electrolyte used as dispersed phase with an HCl solution (0.48 M or 0.97 M). The final HCl concentration of the dispersed aqueous phase was 0.16 M and 0.33 M, respectively. Therefore, the samples were identified by adding the suffix “0.16M” and “0.3M” to the end of the nomenclature. For example, beads produced with the macrofluidic device using the emulsion E12.5-60, which contained a 0.16 M aq. HCl solution as dispersed phase of the emulsion (W_1) were named Mac12.5-60 0.16M.

6.2.3 Preparation of macroporous polymer beads in a macrofluidic plug flow reactor

A simple solution to reduce clogging of the tubings is to increase the distance between the droplets and the tubing walls and therefore minimizing the chance of contact and adhesion of the droplets with the tube wall. Based on that assumption and inspired by the simplicity of the microfluidic approach we designed a macrofluidic plug flow reactor (Figure 6-1). In order to produce emulsion droplets, a W_1/O emulsion was injected into a recirculating secondary aqueous phase (W_2) in a co-flow geometry (Figure 6-1a). A syringe pump (Ultimus IV, NordsonEFD, Pforzheim, Germany) equipped with a 5 ml syringe was used to control the amount of emulsion dispensed through a 22G needle with an internal diameter (I.D.) of 0.41 mm into the carrier phase (W_2). In order to form the co-flow injection, the needle used had a 90° bend.

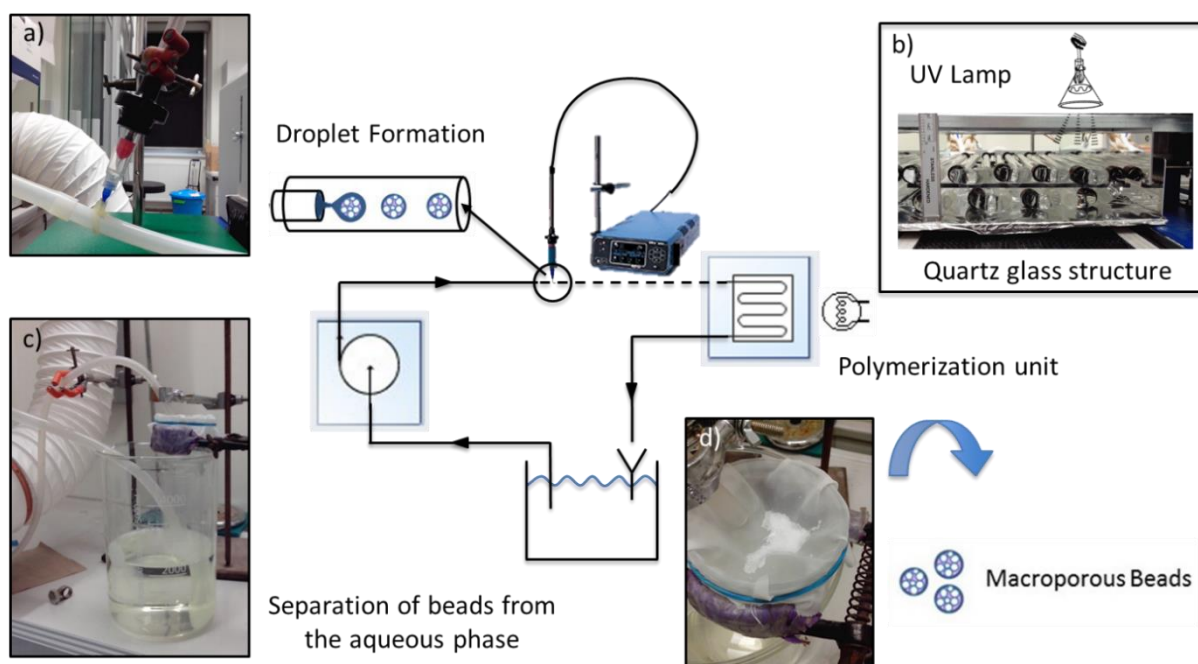


Figure 6-1. Schematic of the macrofluidic plug flow reactor used to produce macroporous beads. The dashed line represents PTFE tubing and the continuous line represents the silicon tubing used. Both tubes had an internal diameter (I.D.) of 12 mm.

The needle was inserted into a 20 cm piece of semi-rigid PTFE tubing (I.D. 12 mm). The tubing was connected to a self-build structure made of interconnected quartz glass tubes (12 mm I.D., total length 760 cm) (Figure 6-1b). The recirculating secondary aqueous or “carrier” phase (W_2) contained poly(vinyl alcohol) (PVA) with an average molecular weight of 30000-70000 g/mol and the surfactant octylphenol ethoxylate (Triton X-405), in a concentration of 3 wt.%, respectively. The secondary aqueous phase was pumped through the tube using a centrifuge pump (Modell WPDC-10.5-5.0M-24-VP, Rotek Handels, Austria). The flow rate of the secondary aqueous phase (W_2) was controlled by regulating the voltage applied to the pump and by a pinch flow valve placed on the silicon tubing 20 cm after the centrifuge pump. To determine the flow rate of the secondary carrier phase (W_2), the time needed to fill a 5 L beaker was measured. In order to polymerise the emulsion droplets formed after injection, the quartz glass structure was placed inside an UV-light curing system (UVC-8 Curing Conveyor System, Dymax Europe GmbH, Wiesbaden, Germany). According to the manufacturer, the maximum intensity of the curing system is 800 mW/cm² for a new bulb working at 60 mm distance from the conveyor belt. The quartz glass structure was mounted on top of a home-built wooden platform clad with aluminium foil to avoid contact with the surface of the conveyor belt. The UV lamp was positioned approximately 100 mm over the quartz glass

structure, providing an irradiation time between 2 min and 8 min to the emulsion droplets, depending on the flow rate of the secondary aqueous phase (W_2). After exposition to UV light the carrier phase (W_2) flowed through a silicon tubing to a 5L beaker, from where it was pumped again into the line creating a closed circuit (Figure 6-1c). At the end of the silicon tubing, a polyester mesh was used as filter to separate the polymerized droplets, i.e. macroporous beads from the carrier phase (Figure 6-1d). As the macroporous beads accumulated on the separator, they were collected regularly using a metal spoon. After removal, the solidified beads were placed overnight in a mixture of ethanol and water (50/50 vol.%) to remove all unreacted chemicals. Afterwards, the samples were stored overnight in distilled water and vacuum dried at 60°C for 12 h. In order to test the ability of the macrofluidic setup to produce beads from emulsion templates with a diverse flow behaviour without clogging, several emulsion templates with different internal phase volume ratios and stabilised by increasing surfactant concentrations were used (Table 6-1).

Table 6-1. Summary of the emulsion template formulations and injection conditions used to test the macrofluidic plug flow reactor. The velocity ratio represents the ratio between the carrier phase and injection velocity.

Formulation	Surfactant concentration ^a [%]	Internal phase volume ratio [%]	Injection flow rate [mL/h]	Injection velocity [cm/s]	Carrier phase flow rate [L/h]	Carrier phase velocity [cm/s]	Velocity ratio
E15-50	15	50	5.4	1.1	20.2	5.0	4.5
E15-70	15	70	5.4	1.1	18.4	4.5	4.1
E15-80	15	80	5.4	1.1	22.3	5.5	5.0
E30-50	30	50	5.4	1.1	14.8	3.7	3.3
E30-80	30	80	5.4	1.1	13.3	3.3	3.0

^a Surfactant concentrations are with respect to monomer phase

6.2.4 Encapsulation of hydrochloric acid in macroporous beads and monoliths

In order to test the encapsulation potential of the macroporous polymers beads produced, two emulsion templates containing aqueous solutions with different HCl concentrations as model molecule (0.16 M and 0.33 M) in the internal phase (W_1) were used to produce beads (Table 6-2). It is worth mentioning that HCl concentrations in the dispersed phase (W_1) higher than 0.33 M caused rapid destabilisation of the emulsion templates. To produce beads with encapsulated HCl, the W_1/O emulsions were injected into the macrofluidic device at different

injection and carrier phase velocity ratios. After polymerisation of the emulsion droplets, the beads were collected and stored in a glass beaker sealed with laboratory film (Parafilm “M”, Oshkosh, USA) at room temperature ($\sim 20^\circ\text{C}$).

Table 6-2. Summary of the emulsion template formulations used for the production of beads and monoliths containing HCl.

Phase of the emulsion	Composition	Sample nomenclature					
		E12.5-60 Cl ₂	E12.5-60 0.16M Cl ₂	E12.5-60 0.33 M Cl ₂	E12.5-60 PT	E12.5-60 0.48M PT	E12.5-60 0.97M PT
W ₁	DI water [mL]	30	29.6	29.2	30	29.6	29.2
	HCl [mL]	0	0.4	0.8	0	0.4	0.8
	CaCl ₂ ·2H ₂ O [g]	0.4	0.26	0.26	0.4	0.26	0.26
O	MMA [mL]	10.5	10.5	10.5	10.5	10.5	10.5
	EGDMA [mL]	7	7	7	7	7	7
	Pluronic L-81 [mL]	2.5	2.5	2.5	2.5	2.5	2.5
	Darocur 1173 [mL]	0.35	0.35	0.35	0.35	0.35	0.35
W ₂	DI water [mL]	5000	5000	5000	5000	5000	5000
	CaCl ₂ ·2H ₂ O [g]	65	65	65	0	0	0
	PVA [g]	0	0	0	150	150	150
	Triton X-405 [g]	0	0	0	150	150	150

Additionally, monolithic polyMIPE samples were prepared following the procedure used in Chapter 4 for the production of compression test samples, the monoliths were also stored in a sealed glass beaker. Periodically, samples were taken, weighted and the concentration of HCl was determined by titration with an aqueous NaOH solution. In order to release the HCl encapsulated, the samples were placed inside a glass beaker with a known volume of distilled water and carefully crushed using a metal spatula. After crushing, one drop of phenolphthalein indicator was added. Known volumes of a 0.01 M NaOH solution were added to the beaker until a slight pink tone was observed, indicating the equilibrium point. After reaching the equilibrium point, the polymer samples inside the beaker were manually stirred with the spatula, in order to allow for complete diffusion of the encapsulated HCl to the NaOH solution. The encapsulation efficiency was calculated following Equation 6-1:

$$\text{Encapsulation efficiency [\%]} = \frac{[\text{HCl}] \text{ Released } [\mu\text{mol/g}]}{[\text{HCl}] \text{ Encapsulated } [\mu\text{mol/g}]} \times 100 \% \quad \text{Equation 6-1}$$

where the released HCl concentration from the beads and monoliths was calculated using:

$$[HCl]_{released} = \frac{[HCl]_{encapsulated} [\mu mol]}{Sample\ mass\ [g]} \quad \text{Equation 6-2}$$

The encapsulated HCl concentration was calculated assuming that the internal dispersed phase (W_1) maintained the HCl concentration prior to polymerisation of the emulsion templates and was calculated as follows:

$$[HCl]_{encapsulated} = \frac{Porosity\ [\%] \times HCl\ conc.\ in\ internal\ phase\ [\mu mol/mL]}{Bead\ density\ [g/mL]} \quad \text{Equation 6-3}$$

6.3 Results and discussion

6.3.1 Synthesis of macroporous beads in a macrofluidic plug flow reactor

In order to compare our macrofluidic setup with a common microfluidic device based on tubing and needles,^{34, 202} beads with a size between 400 and 600 μm were synthesised after polymerisation of W_1/O emulsion droplets. To control the droplet size, the recirculating carrier phase (W_2) velocity was varied while the injection flow velocity was kept constant at 1.1 cm/s (corresponding to a volumetric flow of 5.4 mL/h). The flow conditions used to synthesise the beads along with the bead size, size dispersion and yield are summarised in Table 6-3. The first emulsion tested in the macrofluidic setup was a MIPE, E15-50 with an internal phase volume ratio of 50 % stabilised with a surfactant concentration of 15 vol.%. The emulsion had a viscosity similar to milk. After injection, spherical emulsion droplets formed at the needle tip, leading to macroporous beads with a size of $404 \pm 79\ \mu m$ after polymerisation. Then, the emulsion template E15-70 with an internal phase volume ratio of 70 % and stabilised with a surfactant concentration of 15 vol.% was used. The flow behaviour of this emulsion was similar to milk cream, a bit more viscous than E15-50. The droplets produced using this emulsion were spherical and also formed in the dripping regime, leading to beads Mac15-70 after polymerisation. These beads had the narrowest size distribution of all formulations tested with a coefficient of variation (CV) of 17 %.

Table 6-3. Flow conditions used to produce macroporous beads by macrofluidic polymerisation, the carrier phase velocity was varied to control droplet size. The velocity ratio represents the ratio between the secondary aqueous phase and injection velocities. The bead size coefficient of variation (CV) was the ratio between standard deviation and average bead size.

Beads	Injection velocity [cm/s]	Carrier phase velocity [cm/s]	Velocity ratio	Average bead size [μm]	CV [%]	Yield [%]
Mac15-50	1.1	5.0	4.5	404 ± 79	20	60
Mac15-70	1.1	4.5	4.1	566 ± 99	17	86
Mac15-80	1.1	5.5	5.0	554 ± 103	19	59
Mac30-50	1.1	3.7	3.3	564 ± 122	22	90
Mac30-80	1.1	3.3	3.0	270 ± 12^a	N/A	32
^a 2-3 mm long rods were formed instead of beads						

The emulsion template E15-80 had a flow behaviour similar to milk cream. In this case, the carrier phase velocity was 5.5 cm/s (22.3 L/h). During injection into the macrofluidic device, the droplets formed in the dripping regime (Figure 6-2). After polymerisation, spherical macroporous beads (Mac15-80) with a size of $554 \pm 103 \mu\text{m}$ were obtained.

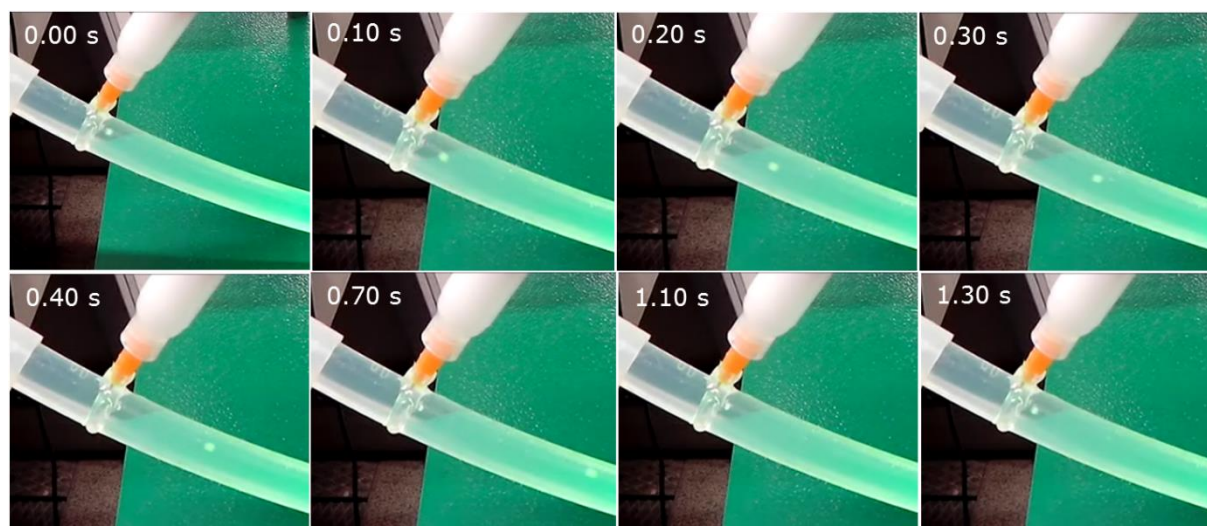


Figure 6-2. Photographs of the formation of emulsion droplets in the dripping regime by injecting the W_1/O emulsion template E15-80.

When the emulsion template E30-50, with a viscosity similar to liquid honey was injected into the carrier phase flowing at 5.5 cm/s (22.3 L/h) a large emulsion thread formed at the needle tip, which increased the size dispersion of the beads formed after polymerisation. Therefore,

it was necessary to adjust the velocity of the carrier phase again. After several attempts, the recirculating carrier phase velocity was set to approximately 3.7 cm/s (14 L/h). With this injection conditions, an emulsion thread of about 4 cm was formed at the tip of the needle, which broke up into non-spherical droplets. These droplets assumed a spherical shape as they flowed downstream with the carrier phase. The produced beads (Mac30-50) had a size of $564 \pm 122 \mu\text{m}$. After injection of the emulsion E30-80 into the macrofluidic device, a thin emulsion thread with an estimated diameter between 200 and 300 μm formed at the needle tip. The emulsion thread broke up into pieces between 2 and 3 mm long. Due to the high viscosity of the emulsion template, similar to thick paint, the shape transition from small sausages into spherical droplets, which was observed for E30-50, was impossible. The droplets kept a rod-like shape. Although several carrier phase velocities were used, none of them allowed for the formation of spherical droplets. When the injection velocity was increased to 11.2 cm/s (54 mL/h), a long thread of more than 10 cm was formed at the needle tip after a few seconds of injection. At a certain point, the emulsion threads detached from the needle tip and polymerised inside the macrofluidic device as large filaments (Figure 6-3a) or rolling on themselves forming clews (Figure 6-3b). To recover this large formations, the carrier phase velocity was increased to 110 cm/s (397 L/h), breaking the structures formed in smaller pieces. However, occasionally large clews (Figure 6-3b) got stuck at the bends of the quartz glass structure requiring to be dismantled and cleaned to remove the obstructions.

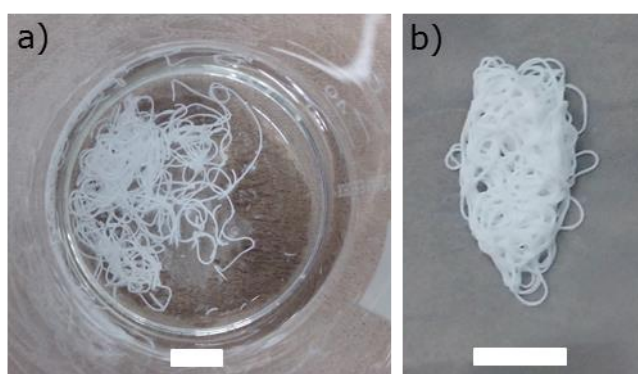


Figure 6-3. Photograph of the polymerized clew formed after injection of E30-80 in the macrofluidic device. The scale bars represents 10 mm.

Despite the different rheological properties of the emulsion templates tested and the high injection flow rates used, no clogging or obstruction of the quartz glass structure or the tubing was observed when individual droplets could be formed.

6.3.2 Size distribution of beads produced by polymerisation of emulsion templates with increasing internal phase volume ratio and surfactant concentration

The bead size distribution obtained after polymerisation of the emulsion droplets is influenced by the viscous drag forces that deform the interface between the emulsion and the carrier phase and interfacial tension forces resisting deformation.²⁴⁶ More importantly, the balance between the two forces will determine the droplet size.²²⁹ Typically, beads with a narrow size distribution, and therefore low coefficient of variation (CV), are obtained if the emulsion droplets are generated at the needle tip in the dripping regime. This was observed for beads Mac15-50, Mac15-70 and Mac15-80, however the bead size CV obtained was around 20 %. During the production of beads Mac30-50, the carrier phase velocity was adjusted to 3.7 cm/s to avoid the formation of a large emulsion thread (Figure 6-2). Using this injection velocity, an emulsion thread of approximately 4 cm formed at the needle tip. The naturally unstable emulsion thread formed during jetting broke up at irregular time intervals into main droplets and much smaller “satellite” droplets.³¹²⁻³¹³ This irregular emulsion droplet formation is typical of jetting regimes, causing the size dispersion of beads Mac30-50 to increase, reaching a CV of 22 %. The difference in bead size distribution compared with typical tubing based microfluidic devices (CV between 8 and less than 1 %) can be explained by the fluid flow behaviour. The low flow velocities and small length scales of microfluidic devices allow these systems to operate in laminar flow conditions, with $Re \ll 1$. In comparison, the Reynolds number of the secondary carrier phase (W_2) used in the macrofluidic device was in the order of 100. While this value of Re is below the transition zone of laminar to turbulent flow, the higher shear forces produced by the carrier phase (W_2) and small perturbations produced by the needle in the laminar flow, known as Kármán vortices³¹⁴ (typical for Reynolds numbers between 40 and 200)³¹⁵ appeared to increase the bead size distribution. Further analysis of the relation between the bead size coefficient of variation (CV) and the different flow rates used is presented later in this chapter.

6.3.3 Production yield of macroporous beads in a macrofluidic plug flow reactor

To increase the bead production rate, an alternative is to increase the emulsion injection flow rate and the carrier phase flow rate. However, this often results in the transition from a dripping to a jetting regime, which increases bead size dispersion. Additionally, the transition to a turbulent flow increases the possibility of droplets coming into contact with the tubing

walls causing clogging of the device. If the system is working in the dripping regime and only the injection flow rate is increased, larger droplets are produced which also increases the chances of clogging the tubing during polymerisation. Due to the larger internal diameter of the tubing used (12 mm) compared with tubing used in microfluidic devices (up to 1.6 mm)^{34, 199}, the chances of droplets coming into contact with the tubing walls and clogging the device are minimised, allowing the use of higher injection flow rates. Furthermore, it is also possible to produce larger beads if desired. Macroporous beads synthesised in microfluidic devices based on tubing and needles are commonly produced using emulsion flow rates up to 1 mL/h while the minimum injection flow rate used in the macrofluidic device was 5.4 mL/h. The first emulsion tested was E15-50, which had a rather low viscosity, some of the emulsion injected was destabilised by the shear forces at the needle tip leading to a low yield (60 %). This effect was also observed after the injection of emulsion E15-80, a thicker emulsion compared with E15-50, leading to a process yield of 59 %. In the case of emulsion E30-50 with similar viscosity to E15-80, the carrier phase velocity was reduced to 3.7 cm/s resulting in a yield of 90 %. At constant injection velocity (1.1 cm/s) for all emulsions used, higher carrier phase velocities led to emulsion droplet destabilisation, resulting in poor process yields. This large variation in the production yield can be explained by the different rheological behaviour of the emulsion templates injected into the macrofluidic device and the formation of perturbations or vortices (typical for $40 < Re < 200$) in the carrier phase caused by the increased flow speed.³¹⁵ A simple solution to increase the yield is to reduce the carrier phase velocity, so new tests were performed at lower flow rates. We discovered that for droplets with a size range of 400-500 μm , if the carrier phase velocity was under 2.5 cm/s, the droplets flowed closer to the glass walls, sometimes forming clusters between them or adhering to the tubing walls. If the carrier phase velocity was instantly increased to more than 3 cm/s, the clusters broke and individual droplets formed again. However, if polymerisation advanced beyond a certain point, even at carrier phase velocities above 5 cm/s, it was not possible to break the droplet agglomerations anymore. After approximately 15 min of injection in this conditions, the polymerised agglomerates obstructed the normal flow of droplets, clogging the device. The sedimentation of droplets can be explained by the density difference between the emulsion droplets and the carrier phase (Table 6-4). Typically buoyancy is ignored in microfluidic devices, as it is assumed that the density differences between the injected fluid and the carrier phase are sufficiently small.²¹⁹

Table 6-4. Summary of the emulsion and secondary aqueous phase (W_2) densities used in the plug flow macrofluidic reactor.

Fluid	Density [kg/m ³]
E15-50	1007
E15-70	1009
E30-50	1015
E30-80	1014
E15-80	1011
sn 1.3 wt.% CaCl ₂ (W_2)	1013
sn 3 wt.% PVA + Triton X-405 (W_2)	1060

In the case of our plug flow reactor, at sufficiently slow carrier phase velocities, the drag forces are insufficient to carry the droplets along the quartz tube. At this point, the density differences between the W_1/O emulsion droplets and the carrier phase (W_2), despite being small, have to be considered to avoid the formation of droplet/beads that could potentially clog the tubing.

6.3.4 Morphology of macroporous beads produced by polymerisation of emulsion template droplets in a macrofluidic plug flow reactor

A summary of the internal pore structure of the beads produced including pore size, pore throat size and surface pore throat size of the beads, along with the injection conditions used is presented in Table 6-5. The beads produced by polymerisation of the MIPes E15-50 had a pore size of $13.6 \pm 8.3 \mu\text{m}$ and a pore throat size of $3.7 \pm 1.8 \mu\text{m}$.

Table 6-5. Properties of macroporous beads produced by polymerisation of emulsion templates with increasing internal phase volume ratio and surfactant concentration.

Beads	Surfactant concentration ^a [%]	Internal phase volume ratio [%]	Pore size [μm]	Pore throat size [μm]	Relative pore throat size ^b [%]	Surface pore throat size [μm]
Mac15-50	15	50	13.6 ± 8.3	3.7 ± 1.8	27	3.2 ± 1.4
Mac15-70	15	70	12.9 ± 7.7	3.7 ± 1.3	29	1.8 ± 0.8
Mac15-80	15	80	12.7 ± 7.9	3.4 ± 1.4	27	3.2 ± 1.4
Mac30-50	30	50	2.8 ± 1.4	0.4 ± 0.1	14	No pores formed
Mac30-80	30	80	3.2 ± 1.6	0.9 ± 0.3	28	No pores formed

^a Surfactant concentrations are with respect to monomer phase, ^b Relative pore throat size is the ratio between average pore throat size and average pore size

Increasing the internal phase volume ratio of the emulsion templates from 50 to 80 % (E15-80) resulted in macroporous beads with an average pore size of $12.7 \pm 7.9 \mu\text{m}$ and an average pore throat size ($3.4 \pm 1.4 \mu\text{m}$). While this variation represents approximately 7 % and 8 % in pore size and pore throat size, respectively, the relative pore throat size did not change (27 %). The internal structure of the beads produced is shown in Figure 6-4. After increasing the surfactant concentration used to stabilise the emulsion templates from 15 to 30 vol.%, a significant reduction in the pore size of more than 70 % was observed (Figures 6-4d and e). A reduction of the same magnitude was also seen for the pore throat size. For example, the pore throat size for beads Mac15-50 dropped from $3.7 \pm 1.8 \mu\text{m}$ to $0.4 \pm 0.1 \mu\text{m}$ when the surfactant concentration was increased from 15 vol.% to 30 vol.%. Moreover, no significant variations were observed in the relative pore throat size (Equation 3-8), which was approximately 27 % for all samples, except for beads Mac30-50, which had a relative pore throat size of only 14 %.

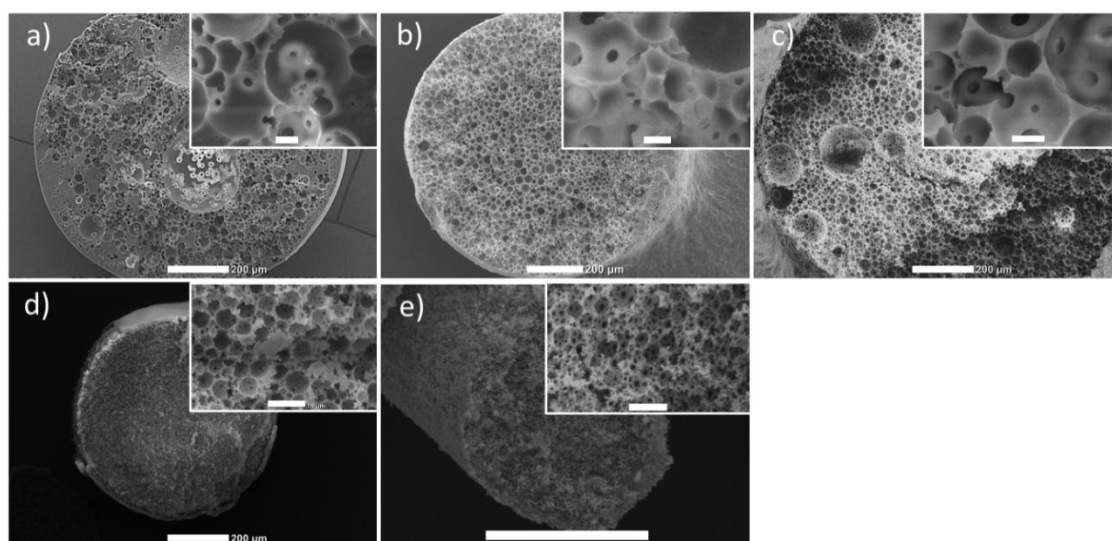


Figure 6-4. SEM images of the cross-section of macroporous beads a) Beads Mac15-50 b) Beads Mac15-70 c) Beads Mac15-80 d) Beads Mac30-50 e) Beads Mac 30-80, in this case rods formed after injection due to the high viscosity of the emulsion template. The scale bar in the images represents 200 μm while the bar in the inserts represents 10 μm .

The surface of the beads produced after polymerisation is shown in Figure 6-5. Beads produced from emulsion templates stabilised with a surfactant concentration of 15 vol.% contained surface pore throats. The formation of surface pore throats was previously observed in Chapter 5 after sedimentation polymerisation of emulsion templates in an aqueous $\text{CaCl}_2 \cdot \text{H}_2\text{O}$ solution. Following a similar mechanism to the formation of internal pore

throats during polymerisation, the droplet continuous phase at the O/W_2 interface shrinks causing ruptures in the polymer film, leading to surface pore throats. Additionally, phase separation of the surfactant occurs in the organic phase due to a decrease of the surfactant solubility as the polymerisation advances, which may also contribute to the formation of superficial pore throats. Beads Mac15-50 had a surface with dispersed surface pore throats with a size of $3.2 \pm 1.4 \mu\text{m}$ (Figure 6-5a). The surface of beads Mac15-70 was more homogeneous with surface pore throats with a size of $1.8 \pm 0.8 \mu\text{m}$ (Figure 6-5b). When the internal phase volume ratio of the emulsion templates was increased to 80 % (E15-80), the surface of the beads produced after injection and polymerisation had homogeneously distributed surface pore throats with a size of $3.2 \pm 1.4 \mu\text{m}$ (Figure 6-5c). As the internal phase volume ratio of the emulsion template increased, the continuous phase between droplets and at the O/W_2 interface becomes thinner, leading to beads with an increased amount of superficial pore throats after polymerisation. The average surface pore throat size in all three cases was in the same size range as the interconnecting pore throats in the interior of the beads. More importantly, an increase in the amount of surface pore throats and, therefore, in the surface interconnectivity was observed after using emulsion templates with increasing internal phase volume ratios.

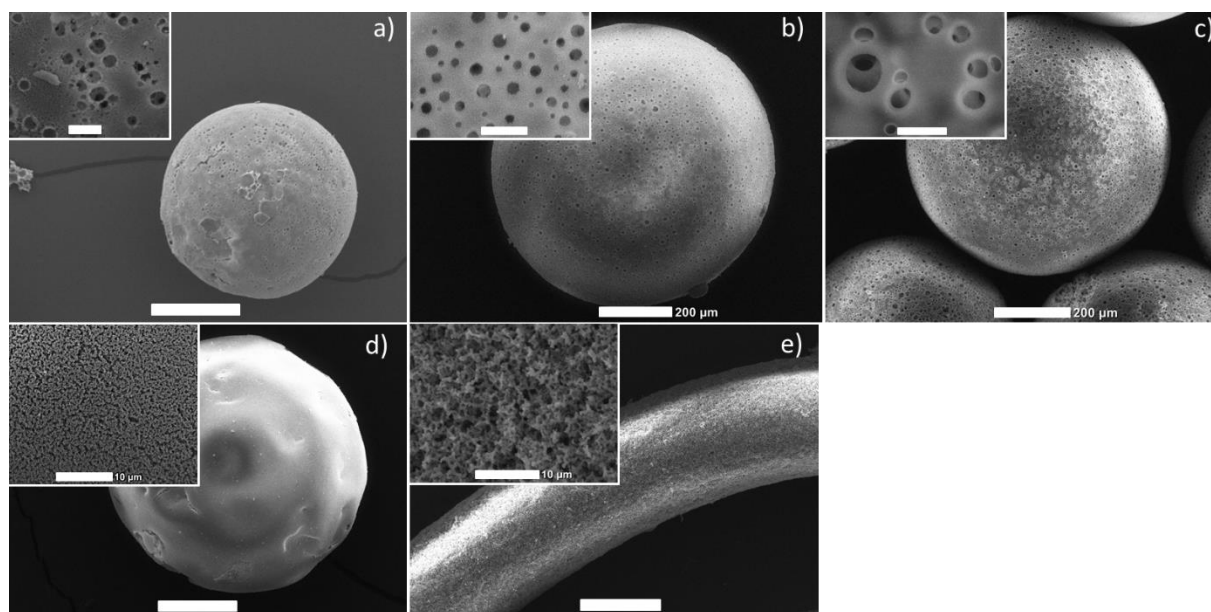


Figure 6-5. SEM images of beads produced by polymerisation of emulsion templates with increasing surfactant concentration and internal phase volume ratios. The scale bar in the images represents 200 μm while the bar in the inserts represents 10 μm .

The surface of beads Mac30-50 changed dramatically, instead of a surface containing well-defined surface pore throats, a porous surface composed of microglobules formed (Figure 6-5d). The transition from a porous to a closed or “skin” surface was studied by Dubinsky et al.²⁷¹ for macroporous poly(GMA-EGDMA) particles by polymerisation in a secondary aqueous phase containing different surfactants. By adding surfactants such as *t*-octylphenoxypolyethoxyethanol (Triton X-100) to the external carrier phase or different solvents to the monomer phase, they controlled the interfacial tension between monomer phase and aqueous carrier phase. Particles with a porous surface were formed when the interfacial tension dropped below a threshold value of 3.0 mN/m. In this case, it is possible that the higher surfactant concentration used in the emulsion templates caused the formation of this kind of bead surface. The surface of rods Mac30-80 formed after polymerization of non-spherical emulsion droplets resembled a collapsed pore structure, also in this case, no superficial pores were observed (Figure 6-5e).

6.3.5 Control of bead size and size dispersion

So far, we demonstrated that it is possible to produce macroporous beads by polymerisation of emulsion templates with different rheological properties in our macrofluidic device. The size range of the beads produced was similar to beads obtained by polymerisation of emulsion templates in microfluidic setups based in commercially available tubing and needles.^{199, 219} However, the size dispersion of beads created using this kind of microfluidic devices is usually low with a coefficient of variation (CV) below 5 %, ³⁴ while the CV of beads created in our the macrofluidic device was in the order of 20 %. With the intention to explore the influence of injection and carrier phase (W_2) velocities on bead size, size dispersion, process yield but more importantly in possible clogging of the device, different injection and carrier phase (W_2) velocities were tested. The velocity ratio between the carrier phase and the injection velocities (Equation 6-4) was used as reference to study the influence of viscous drag forces and interfacial tension forces on the characteristics of the droplet formation.

$$\text{Ratio of speed} = \frac{\text{Carrier phase velocity [cm/s]}}{\text{Injection velocity [cm/s]}} \quad \text{Equation 6-4}$$

The W₁/O emulsion template E15-70 was preferred for injection as its viscosity, similar to milk cream, allowed the production of spherical beads after polymerisation with a relatively low size dispersion with a high process yield (Table 6-3). Also, the emulsion was stable for more than 24 h, allowing the production of large volumes of beads. First, the emulsion E15-70 was injected at constant injection velocity of 1.1 cm/s (5.4 mL/h) and the flow rate of the carrier phase was varied (Table 6-6) leading to beads Mac15-70a, b and c. The relation between the injection flow velocity and the carrier phase velocity varied from 6.2 to 2.7. Further attempts to reduce the carrier phase velocity below 2.5 cm/s led to the formation of droplet agglomerates as described above.

Table 6-6. Summary of the injection conditions used to produce beads by polymerisation of emulsion templates E15-70.

Beads	Injection flow rate [mL/h]	Injection velocity [cm/s]	Carrier phase flow rate [L/h]	Carrier phase velocity [cm/s]	Velocity ratio	Jet size [mm]
Mac15-70a	5.4	1.1	25.2	6.2	5.6	~10
Mac15-70b	5.4	1.1	18.3	4.5	4.1	~25
Mac15-70c	5.4	1.1	11.2	2.7	2.5	~20
Mac15-70d	18	3.7	16.6	4.1	1.1	~25
Mac15-70e	54	11.2	27.4	6.7	0.6	>100
Mac15-70f	54	11.2	14.4	3.5	0.3	>100

The velocity ratio was reduced to 1.1 to produce beads Mac15-70d. In this case, the injection velocity was increased to 3.7 cm/s (18 mL/h) in order to increase the production rate of droplets. The carrier phase velocity was increased resulting in the formation of a jet of approximately 25 mm. After polymerisation of the emulsion templates droplets, spherical beads Mac15-70d were obtained. For beads Mac15-70e and Mac15-70f the velocity ratio between carrier phase and injection was reduced to 0.6 and 0.3, respectively. In both cases a threat of emulsion of more than 100 mm in length formed. The bead size and size dispersion of all beads produced along with the process yield obtained after polymerisation of the emulsion droplets are presented in Table 6-7.

Table 6-7. Summary of the velocity ratios used and the size and size dispersion of the beads obtained along with the yield. A significant variation in the internal morphology of the beads obtained due to the different injection conditions used was not evident.

Beads	Velocity ratio	Average bead size [μm]	CV [%]	Yield [%]	Pore size [μm]	Pore throat size [μm]	Relative pore throat size ^a [%]
Mac15-70a	5.6	444 ± 98	22	58 ± 5	12.7 ± 7.9	3.5 ± 1.3	28
Mac15-70b	4.1	566 ± 99	17	86 ± 6	12.9 ± 7.7	3.7 ± 1.3	29
Mac15-70c	2.5	674 ± 162	24	77 ± 2	13.3 ± 7.8	4.3 ± 1.4	32
Mac15-70d	1.1	717 ± 202	28	82 ± 2	13.7 ± 8.9	3.6 ± 1.1	26
Mac15-70e	0.6	1819 ± 463	25	66 ± 6	14.7 ± 9	3.1 ± 0.9	21
Mac15-70f	0.3	2176 ± 1089	50	83 ± 4	16.8 ± 9.9	3.5 ± 1.3	21

^a Relative pore throat size was calculated as the ratio between average pore throat size and average pore size

Controlling bead size and size dispersion by varying the velocity ratio

Beads Mac15-70a and b were produced with the highest velocity ratios and had the lowest size and size dispersion with a CV of 22 and 17 %, respectively. When droplets were produced using a velocity ratio of 0.6 and 0.3, an emulsion thread of more than 100 mm formed at the needle tip. The jet of emulsion broke at different time intervals, resulting in large elongated droplets, which after polymerisation resulted in beads with an average size of approximately 2 mm (Figure 6-6).

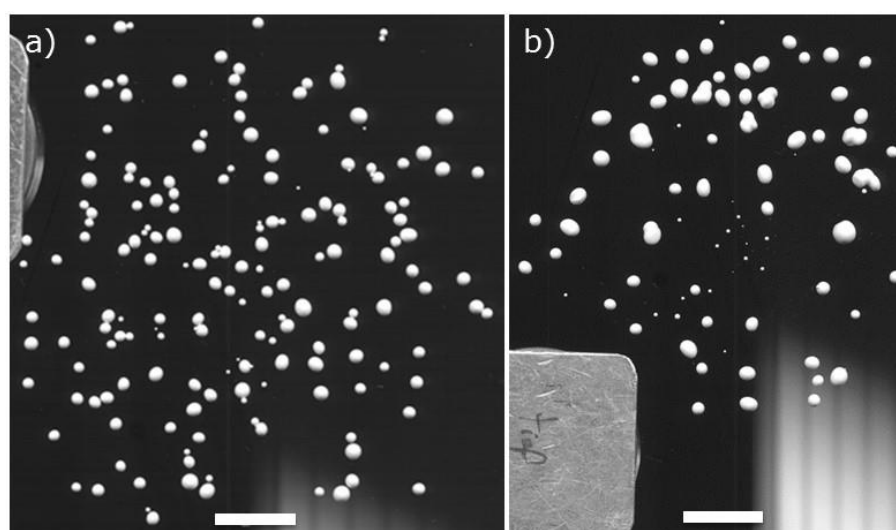


Figure 6-6. Images of beads produced with a velocity ratio below one. The large droplets produced were unable to recover a spherical shape before polymerisation. a) Beads Mac15-70e and b) Beads Mac 15-70f. The scale bars represents 10 mm.

While the size coefficient of variation (CV) of beads Mac15-70e was 25 %, beads Mac15-70f produced with a velocity ratio of 0.3 had a CV of 50 %. This broad size dispersion was caused by the inability of the elongated droplets to assume a spherical shape after detachment from the emulsion thread. On the other hand, all beads produced with a velocity ratio above one were spherical. The influence of the velocity ratio between the injected emulsion and the carrier phase on the size distribution of the beads produced is presented in Figure 6-7. Beads produced at a velocity ratio of 0.6 and 0.3 had a broad size distribution with several size peaks (Figure 6-7a). In contrast, beads produced using a velocity ratio of 4.1 and 2.5 had a narrower size distribution with only one peak at 566 and 674 μm , respectively. The size distribution of beads produced with a velocity ratio between 1.1 and 5.6 is presented in Figure 6-7b. Despite the fact that all beads were produced from emulsion droplets formed in a jetting regime, control of the size dispersion was possible. The narrowest bead size distribution was obtained at a velocity ratio between 4.1 and 2.5.

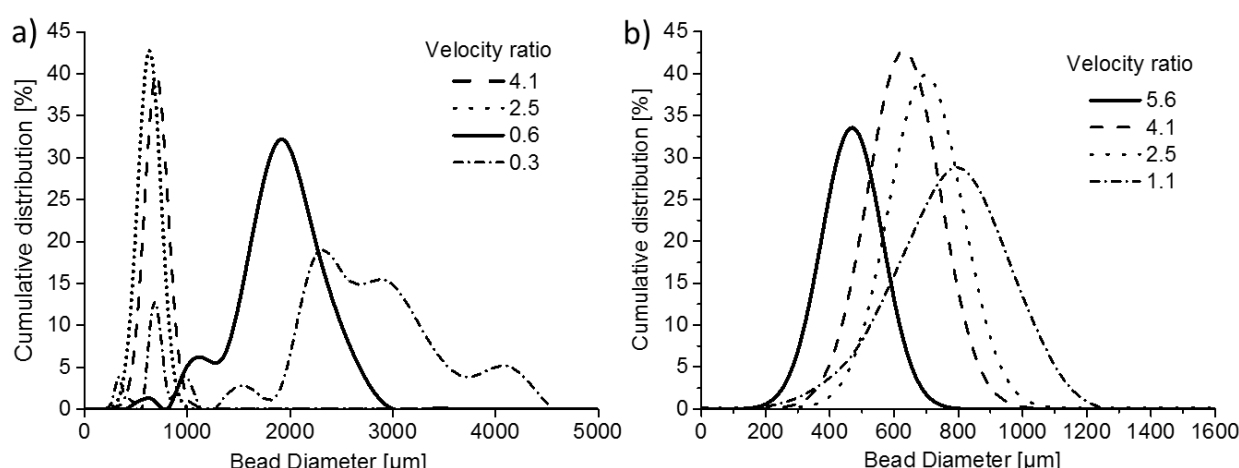


Figure 6-7. Size distribution of beads produced by polymerisation of emulsion template droplets E15-70, formed at various velocity ratios. Below a velocity ratio of 1, control of the size dispersion is lost due to flow turbulence during droplet breakup.

Beads Mac15-70a produced at a velocity ratio of 5.6 had a pore size of $12.7 \pm 7.9 \mu\text{m}$. In comparison, Beads Mac15-70e and f, which were produced at a velocity ratio of 0.6 and 0.3 respectively, had a pore size of $14.7 \pm 9 \mu\text{m}$ and $16.8 \pm 9.9 \mu\text{m}$. This represents an increase in pore size of approximately 16 % for beads Mac15-70e and 32 % in case of beads Mac15-70f. The relative pore throat size of all samples varied from 21 to 32 %. Taking into account that the samples were produced from the same emulsion batch, no major differences were

expected in pore and pore throat sizes after varying the velocity ratio (Table 6-7). However, it is possible that the difference in pore size was due to the turbulence after injection into the secondary aqueous phase (W_2) at a jetting regime, which may promoted destabilisation of the emulsion template droplets.

Production yield of macroporous beads with different velocity ratios

The carrier phase velocity had an important influence on the production yield obtained. The use of a carrier phase velocity above 6 cm/s (25 L/h) used to produce beads Mac15-70a (6.2 cm/s) and Mac15-70e (6.7 cm/s), resulted in rather low process yields (below 70 %), which was caused by destabilisation of the emulsion templates by the drag forces created by the carrier phase during the droplet formation and polymerisation. The use of carrier phase velocities between 3 and 5 cm/s produced the highest yields even if the injection velocity was increased. For example, beads Mac15-70f were synthesised using an injection flow velocity 10 times higher than the initial injection flow velocity (an increase from 1.1 cm/s to 11.2 cm/s). The use of a rather low carrier phase velocity (3.5 cm/s) resulted in a process yield of 83 %, this was achieved despite the droplets detached from a large emulsion jet.

6.3.6 Encapsulation of hydrochloric acid (HCl) in macroporous beads produced by polymerisation of emulsion template droplets in a macrofluidic plug flow reactor

In order to form a porous structure with thicker pore walls and increase the ability of the beads to encapsulate an active ingredient, the internal phase volume ratio was reduced from 70 to 60 %. Additionally, with the intention to reduce pore interconnectivity, the surfactant concentration used to stabilise the emulsion templates was reduced to the minimum amount possible to obtain a stable emulsion. The first emulsion templates with an internal volume phase ratio of 60 % were stabilised with surfactant concentration of 10 vol.% with respect to the monomer phase. A few minutes after emulsification was finished clear signs of phase separation were observed. Based on this results, the surfactant concentration was increased to 12.5 vol.%, achieving emulsion templates that showed no signs of destabilisation for at least 20 h after emulsification. In the case of emulsions containing hydrochloric acid, no significant destabilisation of the emulsions containing 0.16 M aq. HCl solution (E12.5-60 0.16M) as dispersed phase was observed. However, emulsion templates containing 0.33 M aq. HCl solution as dispersed phase (E12.5-60 0.33M) were stable at room temperature only for

approximately 2 h. It is worth mentioning that emulsions stored in the refrigerator (6°C) showed no signs of phase separation for at least 9 days. When higher HCl concentrations were used as internal phase of the emulsion templates, severe phase separation was noted already after a few minutes. Beads containing 0.16 M encapsulated HCl were produced by injecting the emulsion templates containing HCl into the microfluidic device using different flow rates (Table 6-8). Due to the low viscosity of the emulsion templates, it was possible to form droplets in a dripping regime at a velocity ratio up to 2, corresponding to an injection velocity of 3 cm/s (14.4 mL/h) and a carrier phase velocity of 6.1 cm/s (22 L/h). After a further decrease of the velocity ratio to 1.8, a small jet of approximately 5 mm in length formed at the needle tip, indicating the transition to the jetting regime. In this case the injection velocity used was 3.7 cm/s, corresponding to an injection flow rate of 18 mL/h. The injection velocity was further increased until a velocity ratio of 0.6, resulted in the formation of short emulsion threads of approximately 10 mm compared with the 100 mm thread formed when emulsion E15-70 was used.

Table 6-8. Flow conditions used for the production of beads by polymerisation of emulsion templates containing 0.16 M HCl solution as dispersed phase.

Beads	Injection flow rate [mL/h]	Injection velocity [cm/s]	Carrier phase used (W_2) ^a	Carrier phase flow rate [L/h]	Carrier phase velocity [cm/s]	Velocity ratio	Jet size [mm]
Mac12.5-60 0.16M	5.4	1.1	IP 1.3%	25	7.1	6.4	0
Mac12.5-60 0.16M	7.2	1.5	IP 1.3%	28	7.7	5.1	0
Mac12.5-60 0.16M	10.8	2.2	IP 1.3%	23	6.4	2.9	0
Mac12.5-60 0.16M	14.4	3.0	IP 1.3%	22	6.1	2.0	0
Mac12.5-60 0.16M	18.0	3.7	IP 1.3%	24	6.8	1.8	5
Mac12.5-60 0.16M	36.0	7.5	IP 1.3%	32	8.8	1.2	10
Mac12.5-60 0.16M	36.0	7.5	IP 1.3%	17	4.9	0.6	10

^a Carrier phase used: IP 0.5%: 0.5 wt.% CaCl₂, IP 1.3%: 1.3 wt.% CaCl₂, DW: distilled water, PVA + Triton: PVA 3 wt% + Triton 3 wt%

After polymerisation, the beads were collected and stored in a sealed glass beaker in the lab at room temperature (Figure 6-8a). After one day, approximately 10 beads were taken from the samples in the sealed beaker and crushed with a spatula in a Petri dish containing 10 mL distilled water. A pH strip was used to measure the pH of the solution showing a change of

colour indicating a pH of 5 (Figure 6-8b) demonstrating that an active ingredient could be successfully encapsulated. In the case of monolithic samples, after polymerisation and demoulding half of the samples were stored in a sealed beaker (Figure 6-8c) while the other half was kept in an open beaker inside a fume hood.

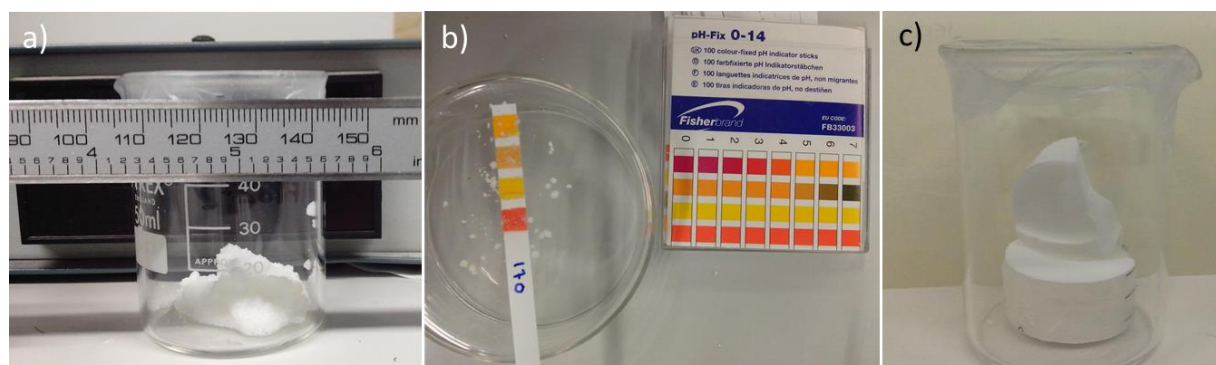


Figure 6-8. Photographs of beads and monoliths obtained after polymerisation of emulsion templates containing 0.16 M HCl aqueous solution as dispersed phase of the emulsion (W_1).

After 24 h in a sealed glass beaker, the amount of HCl encapsulated in the macroporous beads was quantified by titration with 0.01 M NaOH solution. After titration of all the beads produced, the amount of HCl encapsulated was $33 \pm 16 \mu\text{mol/g}$ of bead, representing an encapsulation efficiency of 11 %. The maximum concentration of encapsulated HCl determined was $61 \mu\text{mol/g}$, achieved by using a velocity ratio of 0.6. In this case, the encapsulation efficiency reached was approximately 19 %. In an attempt to increase the amount of HCl encapsulated in the porous beads, the concentration of HCl in the dispersed phase of the emulsion templates used to produce beads was increased from 0.16 M to 0.33 M. The flow conditions used were adjusted to form emulsion droplets in the dripping regime (Table 6-9). After polymerisation and collection, the beads Mac12.5-60 0.33M were stored in a sealed glass beaker. After 24 h, the maximum amount of encapsulated HCl was determined to be $53 \mu\text{mol/g}$ for a velocity ratio of 6.1. The encapsulation efficiency in this case was 8 %, indicating a higher loss of encapsulated HCl than previous beads Mac12.5-60 0.16M. In Chapter 5, the influence of using a carrier phase (W_2) containing PVA and Triton X-405 to reduce the size of surface pore throats in beads produced after polymerisation of emulsion template droplets was described. Therefore, with the intention to increase the amount of HCl encapsulated after polymerisation by reducing the size of the surface pore throats, the

electrolyte used as carrier phase (W_2) was replaced with approximately 5 L of an aqueous solution containing PVA and Triton X-405 (3 wt.%, respectively).

Table 6-9. Flow conditions used for the production of beads from emulsion templates containing HCl 0.33 M solution as dispersed phase.

Beads	Injection flow rate [mL/h]	Injection velocity [cm/s]	Carrier phase used (W_2) ^a	Carrier phase flow rate [L/h]	Carrier phase velocity [cm/s]	Velocity ratio	Jet size [mm]
Mac12.5-60 0.33M	7.2	1.5	IP 1.3%	33	9.1	6.1	0
Mac12.5-60 0.33M	9.0	1.9	IP 1.3%	32	8.8	4.6	0
Mac12.5-60 0.33M	9.0	1.9	IP 1.3%	32	8.8	4.6	0
Mac12.5-60 0.33M	9.0	1.9	IP 1.3%	32	8.8	4.6	0
Mac12.5-60 0.33M	12.6	2.6	IP 1.3%	33	9.1	3.5	0
Mac12.5-60 0.33M	14.4	3.0	IP 1.3%	33	9.1	3.0	0
^a Carrier phase used: IP 0.5%: 0.5 wt.% $CaCl_2$, IP 1.3%: 1.3 wt.% $CaCl_2$, DW: distilled water, PVA + Triton: PVA 3 wt% + Triton 3 wt%							

Beads containing two different concentrations of HCl solution (0.16 M and 0.33 M) as dispersed phase were prepared by polymerisation of emulsion templates in the microfluidic device. First, the emulsion template E12.5-60 0.16M was injected into the carrier phase containing PVA and Triton X-405 using different flow conditions (Table 6-10), which included the transition from the dripping to the jetting regime.

Table 6-10. Flow conditions used for the production of beads by polymerisation of emulsion templates containing 0.16 M HCl solution as dispersed phase. The carrier phase used was an aq. solution containing PVA and Triton X-405 (3 wt.%, respectively).

Beads	Injection flow rate [mL/h]	Injection velocity [cm/s]	Carrier phase used (W_2) ^a	Carrier phase flow rate [L/h]	Carrier phase velocity [cm/s]	Velocity ratio	Jet size [mm]
Mac12.5-60 0.16M	7.2	1.5	PVA+Triton	15.9	4.4	2.9	0
Mac12.5-60 0.16M	7.2	1.5	PVA+Triton	12.2	3.4	2.3	0
Mac12.5-60 0.16M	9.0	1.9	PVA+Triton	12.2	3.4	1.8	0
Mac12.5-60 0.16M	14.4	3	PVA+Triton	15.9	4.4	1.5	10
Mac12.5-60 0.16M	18.0	3.7	PVA+Triton	16.2	4.5	1.2	60
^a Carrier phase used: IP 0.5%: 0.5 wt.% $CaCl_2$, IP 1.3%: 1.3 wt.% $CaCl_2$, DW: distilled water, PVA + Triton: PVA 3 wt% + Triton 3 wt%							

After polymerisation and collection, the amount of HCl encapsulated in the beads was determined. An HCl concentration of $92 \pm 53 \mu\text{mol/g}$ was measured for beads Mac12.5-60 0.16M almost tripling the amount of HCl released from beads produced by polymerisation of emulsion droplets in aqueous CaCl_2 solution. The maximum amount of HCl encapsulated was $144 \mu\text{mol/g}$ for a velocity ratio of 1.2. For this particular velocity ratio, an encapsulation efficiency of 49 % was achieved. While a large deviation in the encapsulation rate was observed, a clear relation between the flow conditions used during bead synthesis and the amount of HCl encapsulated could not be established.

Retention of encapsulated HCl in macroporous polymers

Beads and monoliths were produced using the emulsion templates E12.5-60 0.33M, which contained 0.33 M aqueous HCl solution as dispersed phase of the emulsion template (W_1). After polymerisation the beads were stored in a sealed glass beaker, the same as half of the monolithic samples. The other half of the monoliths produced was stored in an open glass beaker in the fume hood. The amount of HCl encapsulated in beads and monoliths was determined by taking samples regularly, the sealed beakers were open for approximately one min in order to extract the samples. The retention of HCl over time in the macroporous samples produced is shown in Figure 6-9.

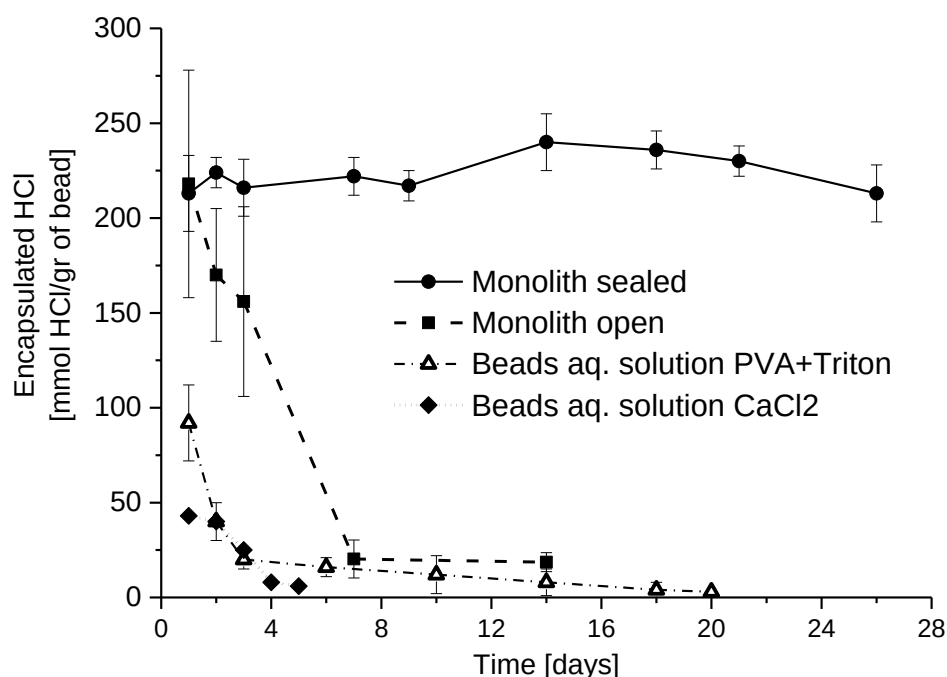


Figure 6-9. Concentration of HCl in monoliths and beads as function of time. The monoliths kept in a sealed glass beaker show a clear improvement in their ability to retain the encapsulated HCl. In the case of the beads, after less than 3 d the concentration of HCl encapsulated dropped significantly.

In the case of monoliths, a clear difference between the samples stored in sealed beakers and samples in an open container was observed. While the initial concentration of HCl was identical for both samples with approximately $219 \pm 20 \mu\text{mol/g}$ (an encapsulation efficiency of almost 40 %), the samples stored in unsealed containers lost HCl rapidly. After 5 d, the HCl concentration was reduced by more than 50 %, while samples kept in the sealed beaker retained the encapsulated HCl for more than 26 days.

In the case of beads, even when they were stored in sealed containers, a significant reduction in the HCl concentration, after 3 days to less than half of the initial HCl concentration, was observed. The large difference in the HCl concentration retained in beads and monoliths can be explained by the diffusion of the active ingredient encapsulated from the W_1/O emulsion template into the aqueous carrier phase (W_2) during bead production in the microfluidic device. The results obtained so far indicate that an active ingredient, in this case HCl, can be encapsulated in macroporous beads and monoliths produced by polymerisation of emulsion templates containing the active ingredient in the dispersed phase of the emulsion templates.

Morphology of macroporous beads and monoliths containing encapsulated HCl

The porosity, pore size and pore throat size of monoliths and beads produced after polymerisation of the emulsion templates E12.5-60 containing different amounts of HCl in the dispersed phase of the emulsion templates is presented in Table 6-11. The monoliths synthesised from emulsion templates without HCl had a porosity of 72 %. Despite the fact that emulsion templates containing HCl were less stable over time, no significant increase in the porosity of the monoliths produced after polymerisation was observed.

Table 6-11. Properties of monoliths and beads obtained after polymerisation of the emulsion templates E12.5-60 containing different amounts of HCl as active ingredients in the emulsion dispersed phase (W_1).

Emulsion template used	Type of sample	Carrier phase (W_2) used ^a	Porosity [%]	Pore size [μm]	Pore throat size [μm]	Relative pore throat size ^b [%]	Surface pore throat size [μm]
E12.5-60	Monoliths	N/A	72%	6.1 ± 3.2	1.2 ± 0.3	20%	N/A
E12.5-60 0.16M	Monoliths	N/A	72%	6.7 ± 4.5	1.6 ± 1.0	24%	N/A
E12.5-60 0.33M	Monoliths	N/A	71%	9.6 ± 14.3	2.0 ± 2.3	21%	N/A
E12.5-60	Beads	IP 1.3%	69%	5.2 ± 3.3	1.1 ± 0.3	21%	1.9 ± 1.1
E12.5-60 0.16M	Beads	IP 1.3%	77%	4.9 ± 2.9	1.0 ± 0.4	20%	2.3 ± 1.7
E12.5-60 0.33M	Beads	IP 1.3%	79%	7.8 ± 7.1	1.6 ± 0.6	21%	2.0 ± 1.2
E12.5-60	Beads	PVA+Triton	60%	5.0 ± 3.3	1.4 ± 0.5	28%	0.9 ± 0.5
E12.5-60 0.16M	Beads	PVA+Triton	70%	7.5 ± 4.4	1.8 ± 0.6	24%	1.4 ± 0.8
E12.5-60 0.33M	Beads	PVA+Triton	72%	6.8 ± 5.1	1.7 ± 0.7	25%	1.9 ± 0.8
^a Carrier phase (W_2) used: IP 1.3%: 1.3 wt.% CaCl_2 , DW: distilled water, PVA + Triton: PVA 3 wt.% + Triton 3 wt.%							
^b Relative pore throat size was calculated as the ratio between average pore throat size and average pore size							

However, a constant increase in the pore size and pore size dispersion of the monoliths produced with higher concentrations of HCl in the dispersed phase of the emulsion templates was noted. This can be easily seen in Figure 6-10, showing the internal structure of monoliths produced by polymerisation of emulsion templates without and with different amounts of aqueous HCl solution. The pore size and size dispersion in monoliths produced by polymerisation of emulsion templates containing an 0.33 M aqueous HCl solution as dispersed phase increased from was $6.1 \pm 3.2 \mu\text{m}$ to $9.6 \pm 14.3 \mu\text{m}$. A similar effect was observed for pore throat size, while monoliths from emulsion templates without HCl had a pore throat size of $1.2 \pm 0.3 \mu\text{m}$, monoliths from emulsion templates containing the aqueous HCl solution (0.33 M) as dispersed phase had a pore throat size of $2.0 \pm 2.3 \mu\text{m}$. This increase in pore throat size promoted the evaporation of encapsulated HCl. Therefore, the HCl concentration notably decreased when the monoliths and beads were placed in an open beaker.

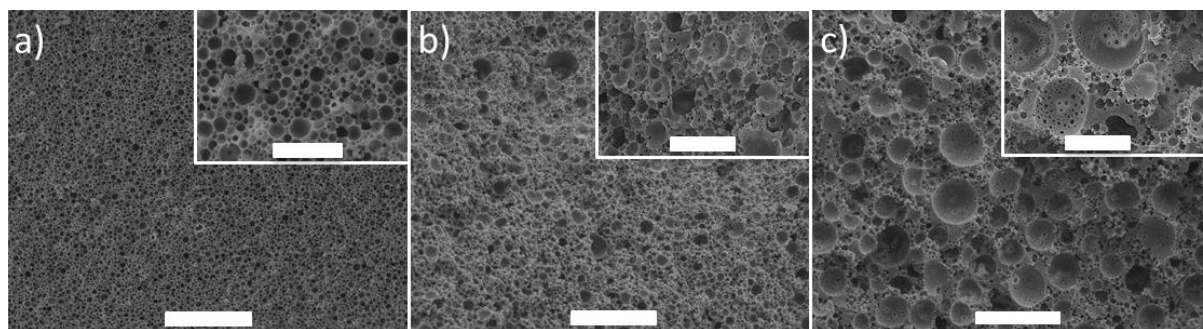


Figure 6-10. SEM images of the internal pore structure of monoliths produced by polymerisation of emulsion templates containing different HCl concentrations in the dispersed phase of the emulsion templates. The scale bars represent 200 μm while the scale bars in the insert represent 50 μm .

In the case of beads, a porosity increase of about 10 % was observed for beads produced from emulsion templates containing HCl. The surface and internal morphology of the beads produced from emulsion templates containing HCl in the dispersed phase of the emulsion templates is shown in Figure 6-11. In the same way as monoliths, the pore size and size dispersion increased after larger amounts of HCl were used in the emulsion templates (Figure 6-11d, e and f). For example, beads obtained after injection and polymerisation of the emulsion E12.5-60 into an aqueous solution containing CaCl_2 had a pore size of $5.2 \pm 3.3 \mu\text{m}$ while the same emulsion containing 0.33 M aqueous HCl solution as dispersed phase (W_1) had an average pore size of $7.8 \pm 7.1 \mu\text{m}$. Similarly to pore size, the pore throat size increased when HCl was encapsulated into the dispersed phase of the emulsion templates. It is worth mentioning that in all samples the relative pore throat size was between 20 and 28 %, independently of the amount of HCl contained in the emulsion template. The surface pore throat size of the beads was reduced by injecting and polymerising emulsion droplets in an aqueous solution containing PVA and Triton X-405 (3wt.%, respectively). The successful modification of the bead surface can be seen in Figure 6-11. In the case of beads produced by polymerisation of emulsion templates without HCl, the size of the surface pore throats was reduced from $1.9 \pm 1.1 \mu\text{m}$ to $0.9 \pm 0.5 \mu\text{m}$. In beads synthesised from emulsion templates containing a 0.16 M aqueous HCl solution as dispersed phase, the size of the surface pore throats was $2.3 \pm 1.7 \mu\text{m}$ after polymerisation in CaCl_2 aqueous solution. When emulsion templates with the same composition were injected and polymerised in an aqueous solution

containing PVA and Triton X-405 (3wt.%, respectively), the size of the surface pore throats was $1.4 \pm 0.8 \mu\text{m}$, a reduction of more than 40 %.

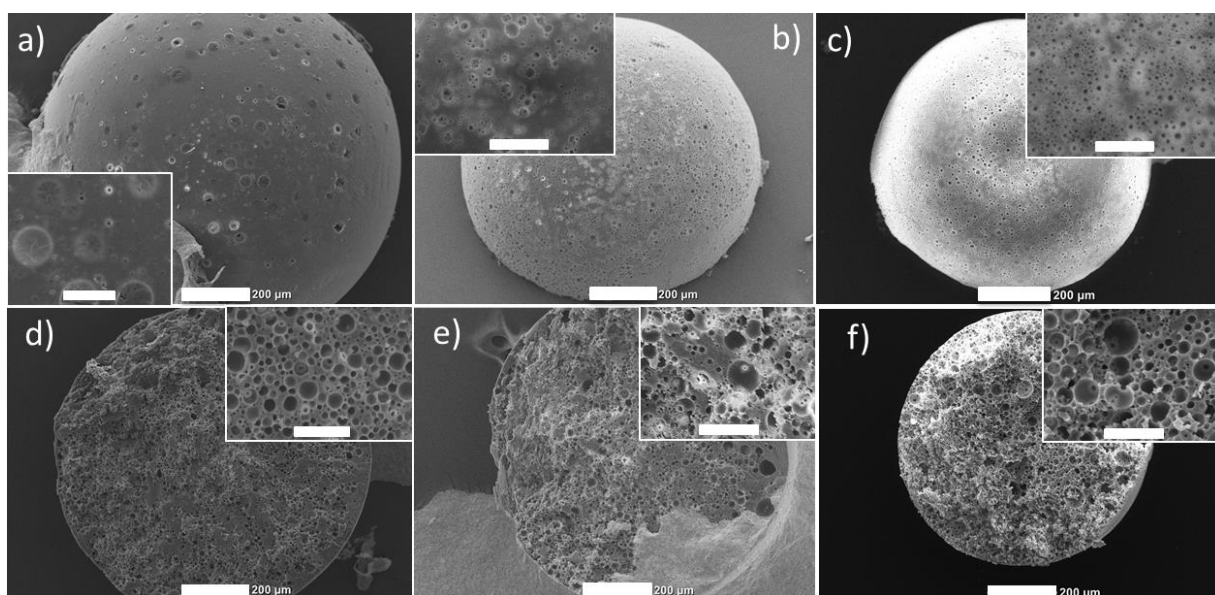


Figure 6-11. SEM images of beads produced by polymerisation of the emulsion templates with increasing amounts of encapsulated HCl in an aq. solution containing PVA and Triton X-405 (3wt.%, respectively). a, d) Beads without encapsulated HCl (Mac12.5-60) b, e) Beads containing 0.16 M HCl aq. solution (Mac12.5-60 0.16M) c, f) Beads containing 0.33 M HCl aq. solution. Scale bars represent 200 μm while bars in the inserts represent 50 μm .

6.4 Summary

An efficient approach for the production of macroporous beads by polymerisation of emulsion templates was developed. Using the macrofluidic plug flow tubular reactor, we managed to scale up the emulsion flow rates commonly used in tubing based microfluidic devices (up to 1 mL/h) to a maximum of 54 mL/h avoiding any kind of clogging and, therefore, increasing the bead production rate.

At the same time we demonstrated that is possible to control the bead size by controlling the (W_1/O) emulsion injection velocity and the recirculating carrier phase (W_2) velocity. The coefficient of variation (CV) of beads produced using the macrofluidic device was in the order of 20 %. Moreover, the transition from the dripping to the jetting regime led to an even larger increase in the bead size dispersion with coefficients of variation above up to 50 %.

Two important restrictions can be observed in the production of macroporous beads in the macrofluidic plug flow reactor. First, as the droplets become larger, the buoyancy forces,

which exponentially increase with the droplet diameter, start to gain more influence in this system. If the droplets are too big or the flow speed of the carrier phase is too low, the drag forces will be insufficient to carry the droplets along the quartz tube leading to the formation of droplet/bead agglomerates which clog the tubing. On the other hand, it was observed that a carrier phase velocity above 5 cm/s led to a reduced yield due to destabilisation of the emulsion templates.

Beads and monoliths containing HCl were synthesised by polymerisation of emulsion templates containing aqueous solutions with different acid concentrations (0.16 M and 0.33 M) as dispersed phase. The encapsulated HCl was released by crushing the porous beads and monoliths. The use of an aqueous carrier phase containing PVA and Triton X-405 (3 wt.% respectively) led to the formation of beads with smaller surface pore throats and higher encapsulation rates. Emulsion droplets containing a 0.16 M aqueous HCl solution as dispersed phase produced beads with a maximum amount of encapsulated HCl of 144 $\mu\text{mol/g}$, representing an encapsulation efficiency of 49 %. However, after 6 days of storage in a sealed beaker, less than 20 % of the initially encapsulated HCl remained inside the beads. Moreover, up to $219 \pm 20 \mu\text{mol/g}$ HCl could be encapsulated in monolithic samples after polymerisation of emulsion templates containing a 0.33 M aqueous HCl solution as dispersed phase, representing an encapsulation efficiency of almost 40 %. The concentration of HCl in the monoliths remained constant for at least 26 days when the samples were stored in a sealed beaker.

Chapter 7. Increasing the encapsulation efficiency in macroporous polymer beads: Production of macroporous beads by printed multi-drop polymerisation

7.1 Introduction

As observed in Chapter 6, two major factors contribute to a low encapsulation efficiency in macroporous beads produced by polymerisation of $W_1/O/W_2$ multiple emulsion templates; i) diffusion of the encapsulated ingredient from the internal dispersed phase (W_1) through the continuous emulsion phase into the secondary aqueous carrier phase (W_2) and ii) the retention of the encapsulated ingredient in the porous bead structure after polymerisation is limited by the permeability of the polymeric layer formed. In order to maximise the encapsulation efficiency and retention of an encapsulated compound within the beads requires the formation of a closed skinned bead surface. The polyHIPE literature detailing the control of the internal pore structure of polyM/HIPE monoliths during polymerisation of emulsion templates is abundant.^{59,135} However, if we focus on pathways to control the outside surface structure of polyHIPEs, most of the literature focuses on polyHIPE membranes and beads, produced by multiple emulsion templating. According to Bhumgara,³¹⁶ the formation of a closed or open outer surface of polyHIPEs produced polymerisation of emulsion templates against a substrate is related to the solubility parameters of the various components involved in the process. If the substrate used is hydrophobic, the surfactant tails will mostly be oriented to the emulsion/substrate interface carrying monomer with them causing the surface layer to become denser and closed than the bulk polyHIPE material, resulting in a closed skin after polymerisation. However, if a hydrophilic substrate is used, surfactant heads carrying water molecules will wet the surface, excluding monomer, which will result in the formation of an open polyHIPE surface with a structure similar to the bulk polyHIPE. Zhao et al.³¹⁷ produced poly(styrene-co-2-ethylhexyl acrylate-co-divinylbenzene)HIPE membranes for electrode applications by polymerisation of the emulsion templates between PTFE films. The membranes had a surface that resembled the interconnected pore structure typical of polyHIPEs. However, emulsion templates with the same formulation when polymerised between glass plates led to polyHIPE membranes with a surface containing some non-porous

areas. The formation of closed areas at the membrane surface was believed to occur due to interaction of the substrates with the surfactant used to stabilise the HIPEs and the initiator potassium persulfate (KPS), used in the internal phase of the HIPE. Poly(glycidyl methacrylate-co-ethyleneglycol dimethacrylate-co-ethylhexyl methacrylate)HIPE membranes with an open pore structure were produced by Pulko et al.³¹⁸ after polymerisation of emulsion templates between glass plates.

Increasing the encapsulation efficiency of macroporous beads produced by polymerisation of W_1/O emulsion template droplets

A simple solution to reduce diffusion of the active ingredient encapsulated in the internal dispersed phase (W_1) to the secondary carrier phase (W_2) before polymerisation may be to avoid the use of an aqueous secondary phase altogether by replacing it by air or an inert gas. The production of macroporous beads by polymerisation of W_1/O emulsion templates in a gas phase has yet to be reported. In this chapter, we tested this approach by polymerising W_1/O emulsion droplets suspended in air. Emulsion templates containing HCl in the dispersed phase were polymerised on different substrates, including a medical grade titanium mesh with the intention to increase the encapsulation efficiency compared to beads produced by macrofluidic polymerisation. Furthermore, the use of different UV sources was tested to initiate photopolymerisation, namely a low intensity hand held UV light and a high-power UV LED. The influence of the UV source on the bead morphology and encapsulation efficiency was studied. Additionally, control beads were produced by sedimentation polymerisation of emulsion templates containing 0.16 M aq. HCl solution as dispersed phase (W_1). The secondary aqueous phase (W_2) used were distilled water and an aqueous solution containing 3 wt.% of PVA and Triton X-405.

7.2 Experimental section

7.2.1 Preparation of the emulsion templates used and nomenclature

Emulsion templates with an internal phase volume ratio of 60 % and 70%, stabilised using 12.5 vol.% and 15 vol.%, respectively, of the non-ionic surfactant Pluronic L-81 were used to produce macroporous beads. Emulsion templates with this composition were successfully used in Chapter 6 to produce HIPEs capable of forming spherical emulsion droplets after injection into a secondary aqueous phase (W_2). The photoinitiator Darocur 1173 was used in

the organic emulsion (O) phase to start the polymerisation after exposure to UV light. The dispersed phase of all the emulsion templates (W_1) used in this chapter consisted of an aqueous solution containing 1.3 wt.% (13.2 g/L) of calcium chloride dihydrate ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$) as electrolyte in order to suppress Ostwald ripening. The organic phase was prepared in a glass reaction vessel (250 mL) fitted with a glass paddle rod (2 blades, anchor shape) connected to an overhead stirrer Heidolph RZR 2102 Control (Heidolph Instruments GmbH, Schwabach, Germany) for 5 min at 500 rpm. Then, the dispersed aqueous phase was added dropwise into the reactor keeping the stirring speed constant. Following addition of the electrolyte, stirring continued for another 10 min to obtain a homogeneous emulsion. A summary of all formulations used can be found in Table 7-1. In order to identify beads produced by polymerisation of multiple emulsion droplets suspended from a Titanium mesh, the prefix “Ti” was included in the nomenclature. Beads produced by sedimentation polymerisation were identified with the prefix “SE”. Additionally, the UV source was also included in the nomenclature, “Dy” was used for beads produced by polymerisation using the UVC-8 Curing Conveyor System, “HH” for beads polymerised using the hand held UV light and “LED” for beads polymerised by exposure to the high-power UV LED. For example, beads from emulsion templates E12.5-60, which had an internal phase volume ratio of 60 %, stabilised using a surfactant concentration of 12.5 vol.% and polymerised using the UVC-8 Curing Conveyor System were called TiDy12.5-60.

Table 7-1. Summary of the nomenclature and emulsion template formulations used to produce beads.

Emulsion phase	Composition	Emulsion nomenclature		
		E15-70	E12.5-60	E12.5-60 0.16M
W_1	DI water [mL]	35	30	29.6
	HCl [mL]	0	0	0.4
	$\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ [g]	0.46	0.4	0.26
Internal phase volume ratio		70	60.0	60
O	MMA [mL]	7.65	10.5	10.5
	EGDMA [mL]	5.1	7.0	7.0
	Pluronic L-81 [mL]	2.25	2.5	2.5
	Darocur 1173 [mL]	0.30	0.4	0.4
Surfactant concentration ^a [%]		15	12.5	12.5
^a Surfactant concentrations are with respect to the monomer phase				

Emulsion templates E12.5-60 containing a 0.16 M aq. HCl solution as dispersed phase (W_1) were used. In this case, the samples produced were identified by adding the prefix “0.16M” at the end of the nomenclature.

7.2.2 Synthesis of macroporous beads by polymerisation of printed multiple emulsion droplets on different substrates

A 5 ml syringe was filled with approximately 4 mL of emulsion template and equipped with a straight 22 gauge needle (I.D. 0.41 mm) at the end. In order to form droplets and then beads after polymerisation, 0.02 mL of emulsion were dispensed at 0.005 mL/s onto different substrates using a syringe pump (Ultimus IV, NordsonEFD, Pforzheim, Germany) holding the 5 ml syringe. The materials used as substrates were kitchen aluminium foil (Folio, Alufix GmbH, Wiener Neudorf, Austria), a glass Petri dish (soda-lime glass, Sigma-Aldrich, Vienna, Austria), backing paper (Folio, Alufix GmbH, Wiener Neudorf, Austria), a 0.5 mm thick PTFE sheet with round holes of 2 mm diameter (Sigma-Aldrich, Vienna, Austria), screen printing mesh (mesh size 32T, polyester) and hexagonal polyester mesh with a side length of ~ 1.5 mm (cell surface ~ 9 mm²). Additionally, two metal substrates were tested, a self-made copper wire mesh (O.D. 0.1 mm, Pengg Kabel GmbH, Kapfenberg, Austria) with cells of 1.5 mm in diameter and a medical grade titanium mesh (100 x 100 mm, Synthes GmbH, Zuchwil, Switzerland). Emulsion droplets were produced by injecting 0.018 mL of emulsion at 0.03 mL/s into the cells of the self-made copper wire (Figure 7-a) and Titanium mesh (Figure 7-b). The injection was performed from the top into the cells of the reticulated substrates, creating emulsion droplets that remained “suspended” from the mesh.

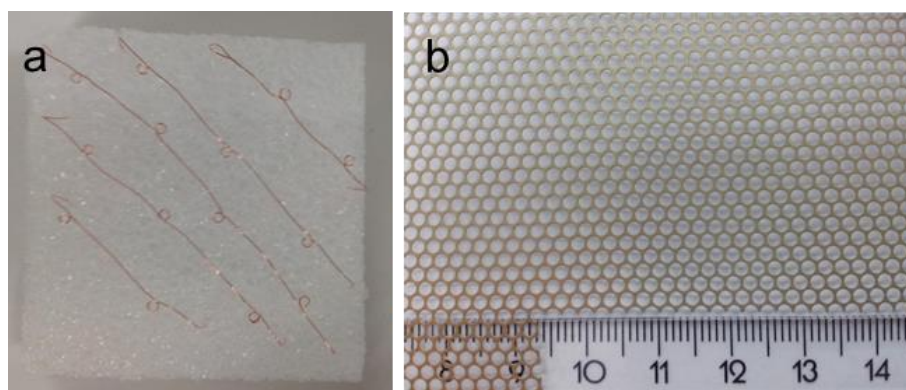


Figure 7-1. Photographs of a) self-made copper mesh and b) Medical grade titanium mesh (TiCP) used to suspend emulsion droplets. The emulsion was injected through the holes in the mesh forming “hanging” emulsion droplets.

After dispensing the emulsion, the substrates containing the droplets were carefully placed under UV light in order to polymerise the suspended droplets to produce solid macroporous polymer beads. Different UV light sources, namely a UVC-8 Curing Conveyor System (Dymax Europe GmbH, Wiesbaden, Germany), a 100 W mercury hand held UV light (UVP Blak-Ray B100AP, 365 nm) and a high-power UV LED (Gröbel GmbH, Ettlingen, Germany) with a maximum irradiance of 25 W/cm² were used. The UVC-8 was used at 90% of intensity and the distance between the samples and the conveyor belt was 180 mm. The conveyor belt speed was kept constant at 1.1 m/s providing an approximate irradiation time of 1 min per run, each sample was placed onto the conveyor belt a minimum of 4 times. After polymerisation, the solidified samples were removed by simply bending the substrate or by gently pushing the beads out of the mesh using a metal spatula. Then, the beads were collected and placed overnight in an ethanol water solution (50/50 vol.%) to remove all unreacted chemicals. In order to complete purification, the samples were left overnight in distilled water after which they were vacuum dried at 60°C for 12 h.

7.2.3 Encapsulation of hydrochloric acid in macroporous beads produced by polymerisation of multiple printed droplets

W₁/O emulsions templates (E12.5-60 0.16M) with an internal phase volume ratio of 60 % containing 0.16 M aq. HCl solution as dispersed phase, stabilised with a surfactant concentration of 12.5 vol.% were used to produce macroporous beads with encapsulated HCl. The beads were synthesised by polymerisation multiple printed droplets using different UV sources, namely a UVC-8 (Curing Conveyor) System, a mercury hand held UV light (UVP Blak-Ray B100AP, 365 nm) and a high-power UV-LED with a maximum irradiance of 25 W/cm². The UVC-8 was used at 90 % of intensity and the distance between the samples and the conveyor belt was 180 mm. The conveyor belt speed was kept constant at 1.1 m/s providing an approximate irradiation time of 1 min per run. Beads Ti-Dy were produced by dispensing 0.015 mL of W₁/O emulsion template at 0.0025 mL/s into the cells of the titanium mesh. The suspended droplets were exposed to UV light for different amounts of time using the UVC-8 Curing Conveyor System (Table 7-2). It is worth mentioning that the printing larger emulsion volumes into the mesh resulted in the detachment of the droplets from the titanium mesh due to their own weight.

Table 7-2. Summary of the emulsion templates formulations and exposure to UV light used to produce macroporous beads (TiDy).

Beads	Emulsion used	Substrate used	UV light used	Exposure
TiDy-1	E12.5-60	TiCP Mesh	Dymax	5 min
TiDy-2	E12.5-60 0.16M	TiCP Mesh	Dymax	2 min
TiDy-3	E12.5-60 0.16M	TiCP Mesh	Dymax	3 min
TiDy-4	E12.5-60 0.16M	TiCP Mesh	Dymax	4 min

In the case of droplets irradiated using the hand held UV light and the high-power UV-LED, the polymerisation conditions used are summarised in Table 7-3.

Table 7-3. Polymerisation conditions used for the production of beads from emulsion templates containing HCl 0.16 M solution as dispersed phase (W_1).

Beads	Emulsion used	Polymerisation method	Substrate or carrier phase used	UV light used	UV Exposure
TiHH-1	E12.5-60	Multidrop	TiCP Mesh	HH	60 min
TiHH-2	E12.5-60 0.16M	Multidrop	TiCP Mesh	HH	40 min
TiHH-3	E12.5-60 0.16M	Multidrop	TiCP Mesh	HH	60 min
TiLED	E12.5-60 0.16M	Multidrop	TiCP Mesh	LED	4 min
SEHH-1	E12.5-60 0.16M	Sedimentation	DW	HH	60 min
SEHH-2	E12.5-60 0.16M	Sedimentation	PVA + Triton	HH	40 min

Beads Ti-HH were produced after printing 0.015 mL of emulsion with and without HCl in the dispersed phase (W_1) at 0.025 mL/s into the cells of the titanium mesh. After dispensing the emulsion, the mesh containing the “suspended” droplets was placed at 100 mm under the hand held UV light to initiate polymerisation for various amounts of time. In order to produce beads TiLED, a different printing setup that combined a syringe pump, a high-power UV LED and a desktop 3D printer was used (Figure 7-2a). The “spindle” or system held tool of a Stepcraft-2/420 CNC system (Stepcraft GmbH & Co, Menden, Germany) was replaced by a home-built aluminium platform onto which dispensing syringe and high-power UV LED were mounted. The UV light irradiance and irradiation time were controlled using a personal computer (PC). The movement of the platform was also controlled using this PC using the software WINPC-NC (CNC-STEP e.K., Geldern, Germany). However, these CNC system and the syringe pump worked independently. Emulsion droplets were produced by placing the needle on top of the titanium mesh and dispensing 0.02 mL of emulsion at 0.003 mL/s. After the emulsion volume was dispensed, the formed droplet was irradiated by UV light for 4 min. The

high-power UV LED tip was kept at distance of approximately 25 mm above the titanium mesh at an angle of 70°. The irradiance used to polymerise the emulsion droplets was approximately 0.6 W/cm² in a narrow wavelength range centred around 365 nm (Figure 7-2b).

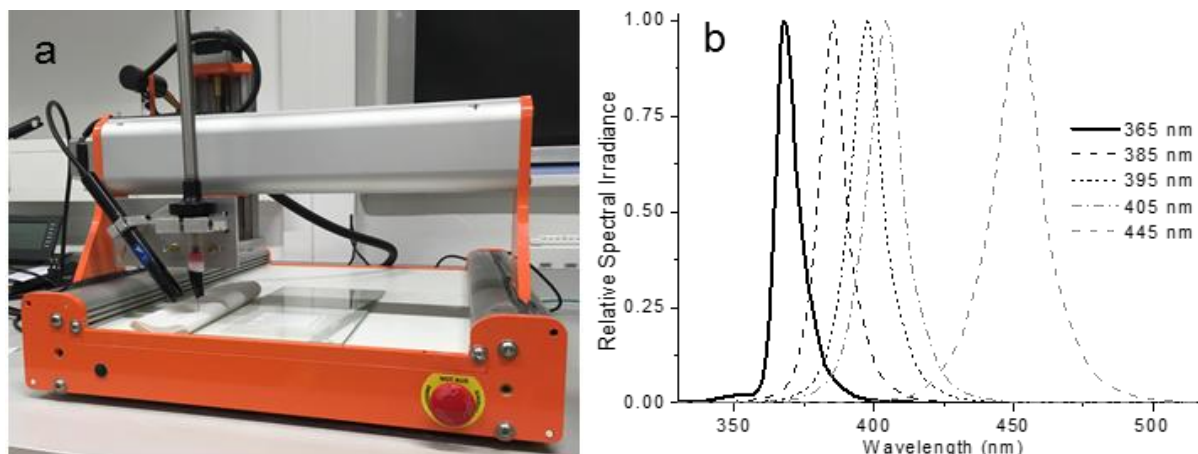


Figure 7-2. a) CNC system including pen UV light and dispensing module used to produce macroporous beads TiLED b) Relative spectral irradiance of pen UV light³¹⁹ used to polymerise TiLED beads, in this case the wavelength used was 365 nm.

After 4 min, the UV light was switched off and the platform with the dispenser shifted to a new position over the titanium mesh and the process was repeated. The entire time required to move the printer head, dispense the emulsion and polymerise each droplet individually was approximately 4.5 min. After polymerisation, the beads formed on the titanium mesh were released by applying a slight pressure with a metal spoon. Beads SEHH were produced by sedimentation polymerisation of emulsion template droplets (E12.5-60 0.16M) in distilled water (SEHH-1) and an aqueous solution containing 3 wt.% of PVA and Triton X-405 (SEHH-2). After injection, the emulsion droplets were polymerised using the hand held UV light for various amounts of time.

All beads containing HCl were collected and stored in a glass beaker sealed with laboratory film (Parafilm "M", Oshkosh, USA) and stored at room temperature (~20°C). The amount of HCl encapsulated in the macroporous beads was quantified by titration with 0.01 M NaOH solution, following the procedure used in chapter 6.2.4. Additionally, the encapsulation efficiency was calculated using Equation 6-1.

7.3 Results and discussion

7.3.1 Macroporous beads produced by polymerisation of multiple droplets printed on different substrates

The emulsion template E15-70 containing an internal phase volume ratio of 70 % stabilised with a surfactant concentration of 15 vol.% was dispensed onto different substrates in order to produce emulsion droplets, which after polymerisation resulted in macroporous beads. Following the printing of emulsion droplets onto aluminium foil, glass and PTFE film substrates, spreading of the emulsion on the substrate surface was observed due to the fact that the low surface tension oil phase was the continuous phase and the relatively low viscosity of the emulsion template used (Figure 7-3 a,b and c). During the polymerisation of the emulsion droplets dramatic phase separation occurred. Therefore, it was decided to explore other substrates, such as baking paper and different kinds of polymer meshes for the production beads.

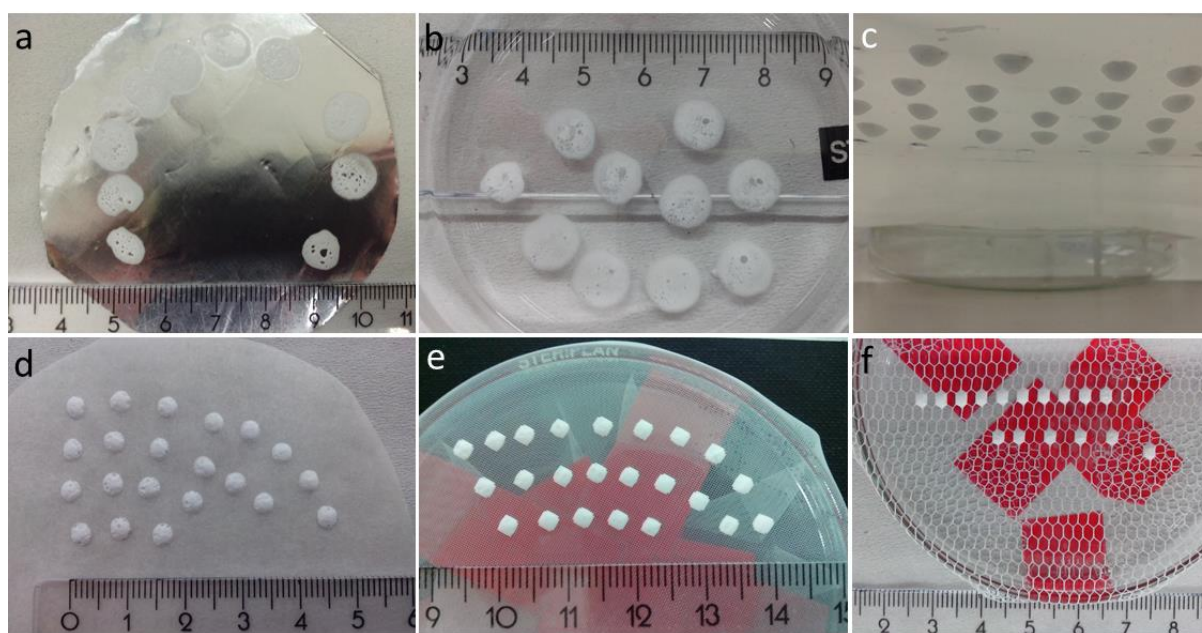


Figure 7-3. Photographs of macroporous polymer beads produced by polymerisation of emulsion droplets (E15-70) printed on a) aluminium foil, b) glass Petri dish, c) PTFE mesh, d) baking paper, e) screen printing mesh 32T, and f) polyester mesh.

On the three of the substrates tested, the spreading of the emulsion droplets after printing resulting in an increased wetted area was dramatically reduced (Figure 7-4). After polymerisation of the printed droplets semi-spherical macroporous polymer beads were obtained. It is worth mentioning that no spreading was observed after printing the emulsion

template droplets into the hexagonal polyester mesh (Figure 7-3f). In this case, the filaments of the mesh hindered spreading the emulsion droplets, so when increasing the emulsion volume further, pendent emulsion droplets formed and “hang” from the mesh filaments. This lead to the formation of macroporous beads with similar sizes after polymerisation.

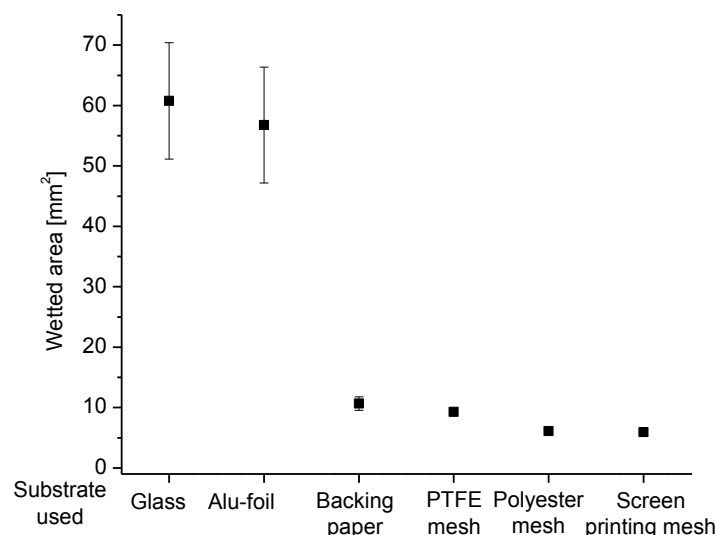


Figure 7-4. Wetted area of emulsion droplets on various substrates as result droplet spreading after printing 0.01 mL of emulsion.

After polymerisation of the printed emulsion template droplets, the resulting beads had an open pore surface (Figure 7-5). Beads BP-Dy printed and polymerised on backing paper, had surface pore throats with an average size of $4.5 \pm 3.9 \mu\text{m}$ (Figure 7-5a). Beads PTFE-Dy produced after polymerisation on a PTFE sheet, had surface pore throats with an average size of $5.7 \pm 3.5 \mu\text{m}$ (Figure 7-5b). The beads MeDy-1 and 2 produced after polymerisation of emulsion droplets suspended from polyester mesh with hexagonal cells and screen printing mesh had surface pore throats with an average size of $4.4 \pm 3.5 \mu\text{m}$ and $5.5 \pm 3.9 \mu\text{m}$, respectively. No significant differences were observed in the average surface pore throat size of all beads produced after polymerisation of emulsion droplets on the various substrates tested. However, a smaller amount of surface pore throats was observed on beads created after polymerisation of pendent emulsion droplets suspended from the polyester meshes (Figure 7-5c and d). This is likely due to the reduced contact area between the emulsion template and the mesh compared to droplet printed on backing paper and PTFE mesh, which may have promoted the destabilisation of the emulsion templates. An analysis of the internal pore structure of the beads produced (Figure 7-6) revealed a homogeneous pore structure

typical for polyHIPEs. Beads BP-Dy had a pore size of $20.4 \pm 13.7 \mu\text{m}$ with interconnecting pore throats of an average diameter of $3.9 \pm 2.4 \mu\text{m}$ (Figure 7-6a).

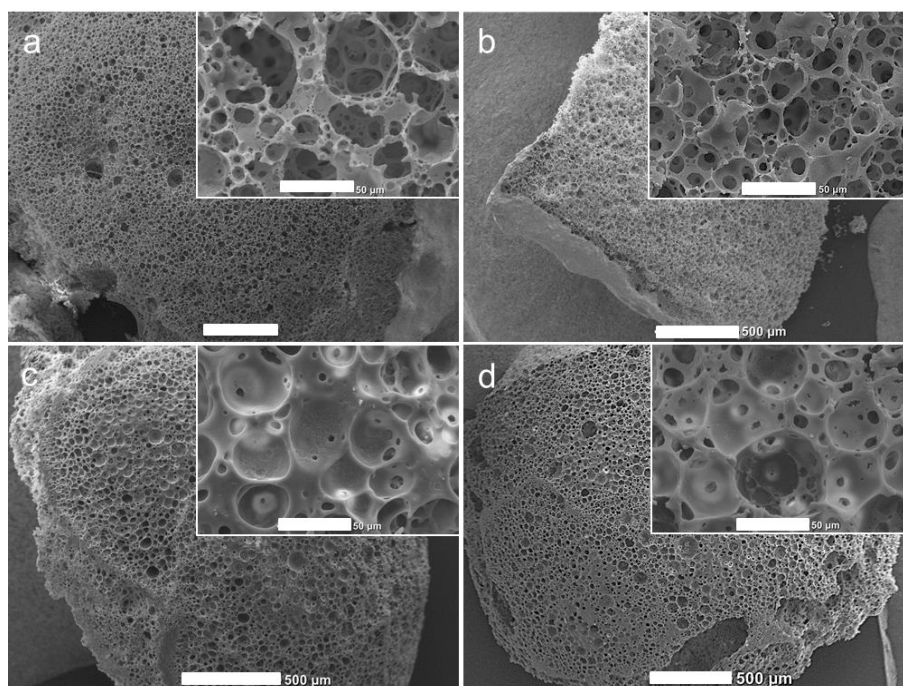


Figure 7-5. SEM images of beads produced by polymerisation of emulsion E15-70 droplets printed on a) baking paper (BP-Dy beads), b) PTFE sheet (PTFE-Dy beads), c) hexagonal polyester mesh (MeDy-1), and d) 32T polyester screen printing mesh (MeDy-2). Scale bars are 500 μm and 50 μm for the inserts.

The average porosity of the macroporous polymer beads produced by polymerisation of multiple droplets printed onto various substrates was 85%, which was significantly higher than expected when using an emulsion template with an internal phase volume ratio of 70%. The high porosity of the beads can be explained by a loss of organic phase from the emulsion due to evaporation prior to polymerisation or an incomplete polymerisation of the organic phase due to inhibition by oxygen. Beads PTFE-Dy had an average pore size of $20.8 \pm 12.9 \mu\text{m}$ and pore throats with an average size of $3.6 \pm 1.9 \mu\text{m}$ (Figure 7-6b). The average porosity of these beads was also 85%. The relative pore throat size in beads produced after polymerisation on backing paper and PTFE sheets was approximately 20% in both cases. The internal pore structure of beads MeDy-1 consisted of pores with an average pore diameter of $23.3 \pm 13.2 \mu\text{m}$, which were interconnected by pore throats with an average size of $4.4 \pm 3.5 \mu\text{m}$, resulting in a relative pore throat size of 19%. The beads MeDy-2 produced after polymerisation of emulsion droplets suspended from the hexagonal polyester mesh had an average pore size of $22.7 \pm 16.4 \mu\text{m}$ and a pore throat size of $3.6 \pm 3.1 \mu\text{m}$ (Figure 7-6d).

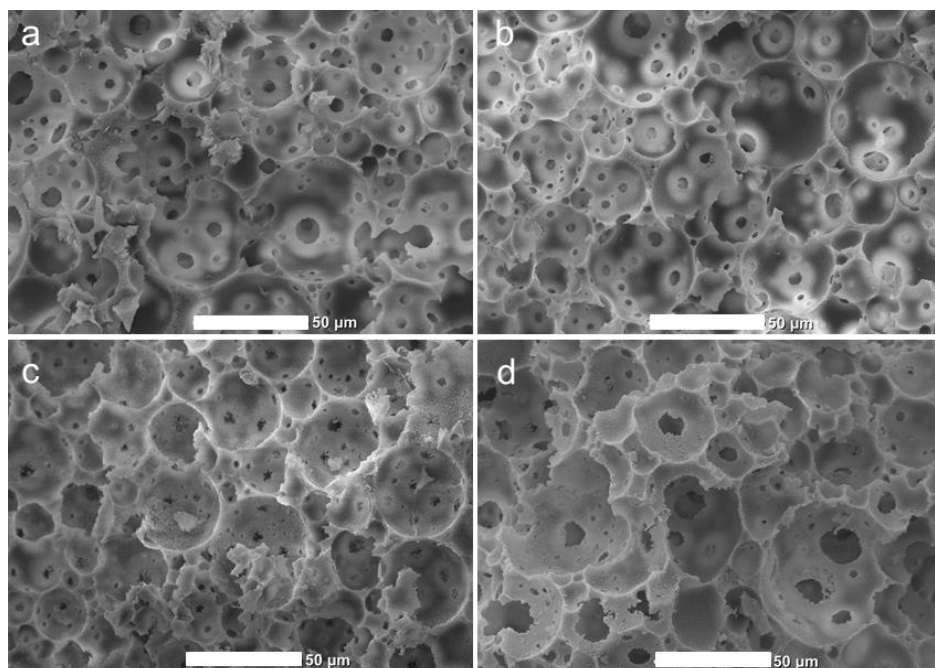


Figure 7-6. SEM images of beads produced by polymerisation of droplets of emulsion template E15-70 printed on a) baking paper b) PTFE sheet c) hexagonal polyester mesh and d) polyester screen printing mesh (32T). Scale bars represent 50 μm .

The pore and pore throat sizes of beads produced by polymerisation of emulsion droplets suspended from the polyester hexagonal mesh were the largest obtained. Their relative pore throat size was 19%, similar to those produced by polymerisation of emulsion droplets printed on baking paper and a PTFE sheet. To summarise, no significant differences were observed in the internal morphology of macroporous beads produced after polymerisation of the emulsion template E15-70 on the different substrates tested (see Table 7-4). All macroporous beads had an average porosity of 85% and their relative pore throat size varied between 16 and 20%.

Table 7-4. Properties of macroporous beads produced by polymerisation of emulsion templates E15-70 printed on different substrates.

Beads	Substrate used	Pore size [μm]	Pore throat size [μm]	Surface pore throat size [μm]	Relative pore throat size [%]	Porosity [%]
BP-Dy	Backing paper	20.0 ± 13.7	3.9 ± 2.4	4.5 ± 3.9	20%	85 ± 2
PTFE-Dy	PTFE sheet	20.8 ± 12.9	3.6 ± 1.9	5.7 ± 3.5	17%	85 ± 1
MeDy-1	Screen printing mesh	23.3 ± 13.2	4.4 ± 3.5	5.5 ± 3.9	19%	85 ± 2
MeDy-2	Hexagonal mesh	22.7 ± 16.4	3.6 ± 3.1	4.4 ± 3.5	16%	85 ± 2

Production of macroporous beads by polymerisation of emulsion droplets suspended from a metal mesh

In order to produce beads of similar sizes by utilising the limited spreading observed when printing emulsion droplets into the cavities of mesh substrates, two different metal meshes were tested. In both cases, after the individual cell surface was filled with emulsion, a rounded pendent droplet was suspended from the mesh (Figure 7-7). These droplets were polymerised. The maximum amount of emulsion that could be suspended from the copper mesh was 0.018 mL; larger emulsion droplets detached from the mesh due to their own weight.

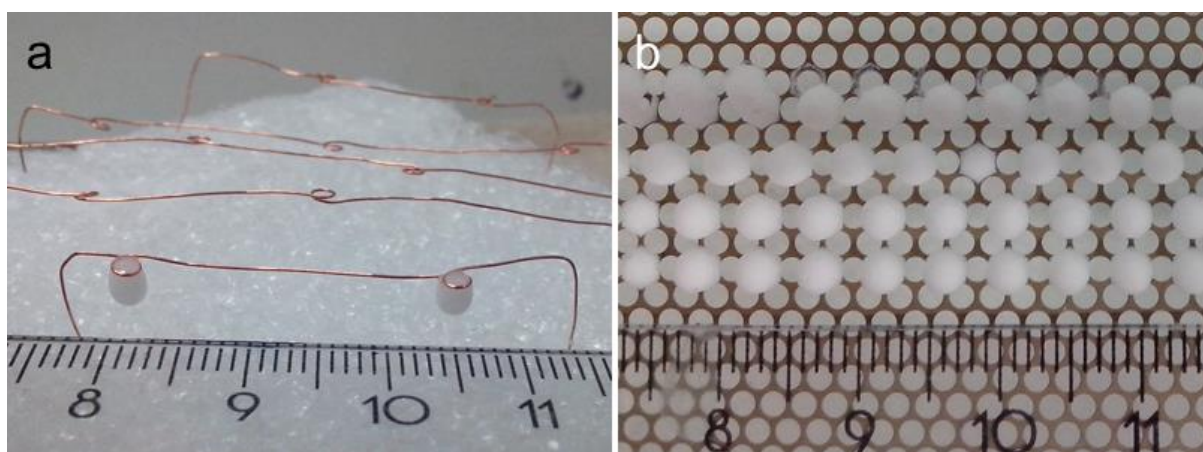


Figure 7-7. Photographs of emulsion droplets suspended from a) self-made copper wire mesh (side) and b) titanium mesh. In this case, the picture was taken from the bottom.

The rounded beads produced by polymerisation of emulsion droplets suspended from the self-made copper mesh had an open pore surface (Figure 7-8a and b) with surface pore throats with an average size of $5.5 \pm 2.4 \mu\text{m}$. The internal structure of the beads consisted of pores with an average diameter of $20.8 \pm 12.7 \mu\text{m}$, which were interconnected by pore throats with an average size of $2.3 \pm 1.0 \mu\text{m}$. The surface pore throat size, pore size and pore throat size were similar to those of beads produced after polymerisation of the template droplets on baking paper, PTFE sheet and polyester meshes (Table 7-4). The average porosity of these beads was also 85%.

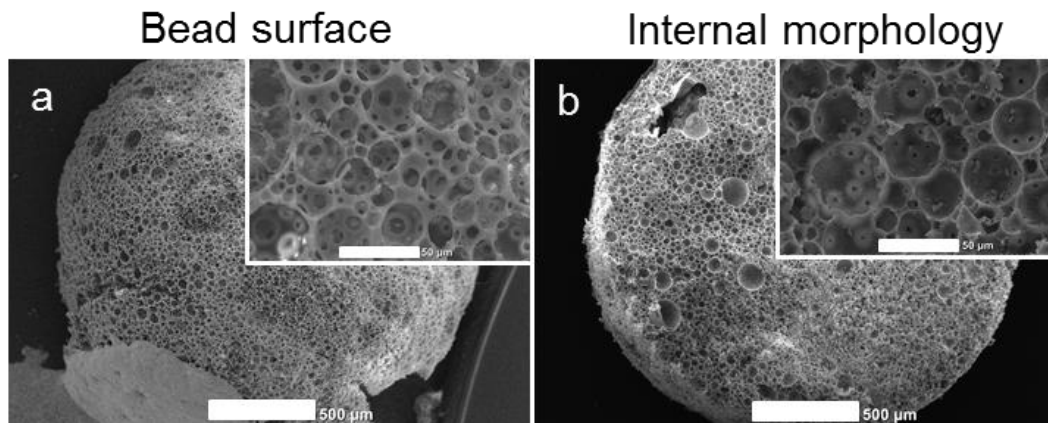


Figure 7-8. SEM images of macroporous beads produced by polymerisation of emulsion templates E15-70 suspended from a self-made copper mesh. Scale bars are 500 μm for images a and c; 50 μm for images b and d, and 10 μm in the inserts.

The bead surface, internal pore structure and surface at the interface with the titanium mesh of macroporous beads produced by polymerisation of emulsion droplets suspended from the titanium mesh is shown in Figure 7-9. The surfaces of the beads, polymerised in contact with air, had surface pore throats with an average diameter of $5.4 \pm 3.1 \mu\text{m}$ (Figure 7-9a). The internal structure of the beads contained pores with average size of $14.1 \pm 10.5 \mu\text{m}$ interconnected by pore throats with an average size of $3.0 \pm 1.6 \mu\text{m}$ (Figure 7-9b). While the average pore size in this case was approximately 30% smaller than previous beads, the relative pore throat size was 21%, which was similar to that of all other beads produced by polymerisation of emulsion template droplets printed on different substrates (Table 7-5).

Table 7-5. Summary of pore size, pore throat size, surface pore throat size and porosity of macroporous beads produced by polymerisation of emulsion templates E15-70 droplets suspended from a self-made copper mesh and a titanium mesh.

Beads	Substrate used	Pore size [μm]	Pore throat size [μm]	Surface pore throat size [μm]	Relative pore throat size [%]	Porosity [%]
CoDy	Copper mesh	20.8 ± 12.7	2.3 ± 1.0	5.5 ± 2.4	11%	85 ± 1
TiDy-0	TiCP Mesh	14.1 ± 10.5	3.0 ± 1.6	5.4 ± 3.1	21%	85 ± 1

The interface between the bead surface and the titanium mesh was close celled (Figure 7-9c). However, during detachment of the beads from the titanium mesh, some parts of the bead

surface remained attached to the mesh revealing the internal pore structure of the beads (Figure 7-9c2).

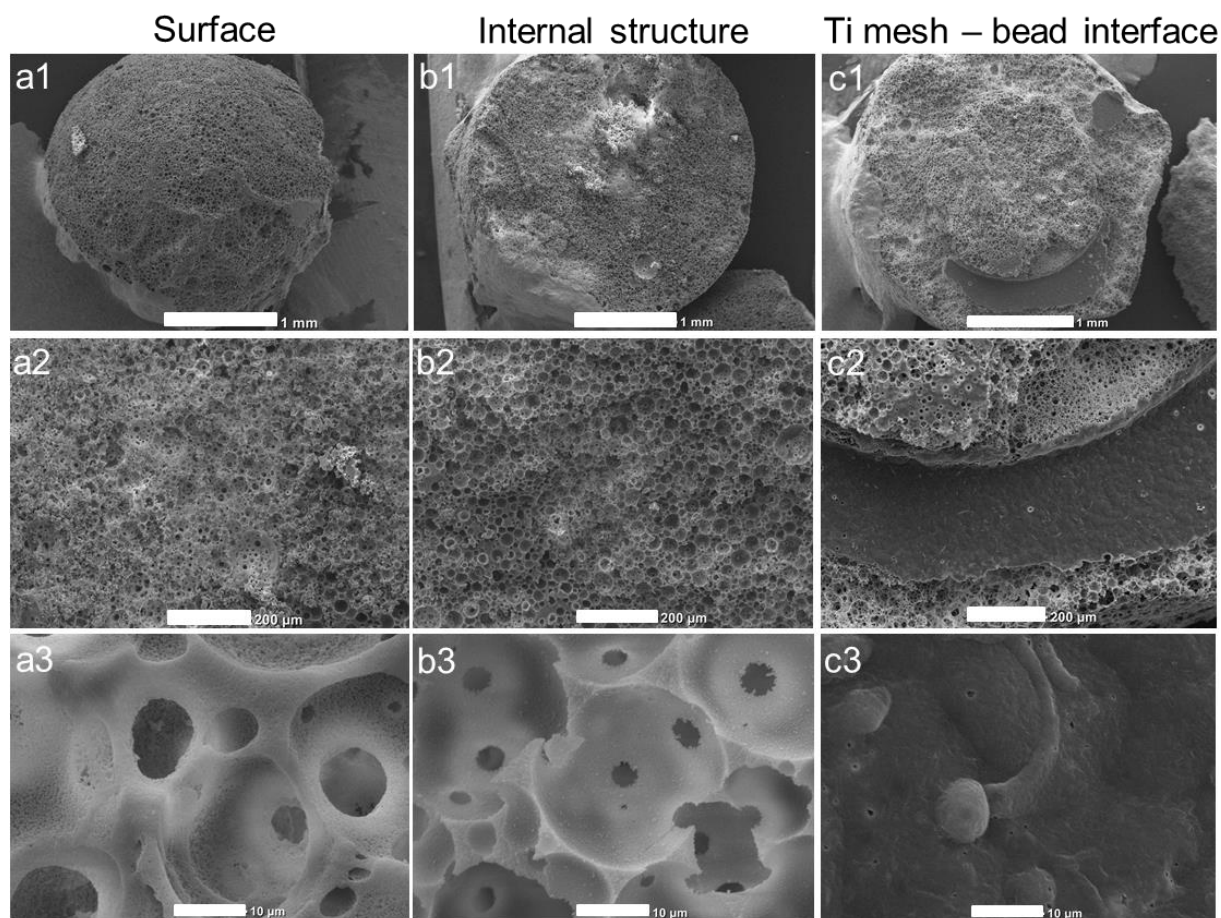


Figure 7-9. SEM images of macroporous beads produced by polymerisation of emulsion droplets (E15-70) suspended in a titanium mesh. An interconnected and homogeneous pore structure was formed inside the beads after polymerisation. Polymerisation of emulsion templates in contact with the titanium mesh resulted in a closed surface. Scale bars are 1 mm (a), 200 μm (b) and 10 μm (c).

7.3.2 Encapsulation of hydrochloric acid (HCl) in macroporous beads produced by polymerisation of multiple printed droplets

In order to produce beads with encapsulated HCl the internal phase volume ratio of the emulsion templates was reduced from 70 to 60% to form a porous structure with thicker pore walls after polymerisation. With the intention to lower the pore interconnectivity, the surfactant concentration used to stabilise the emulsion templates was reduced from 15 vol.% to the minimum possible (12.5 vol.%) to obtain a stable emulsion. Emulsion templates with the same formulation (E12.5-60 0.16M) were previously used in Chapter 6 to produce

macroporous beads containing HCl via macrofluidic polymerisation. The pore size, pore throat size, surface pore throat size and encapsulation efficiency of beads produced after polymerisation of the emulsion templates E12.5-60 with and without HCl in the dispersed phase of the emulsion (W_1) are summarised in Table 7-6.

Table 7-6. Physical properties and encapsulation efficiency of macroporous beads produced by polymerisation of emulsion template droplets containing 0.16 M HCl solution as dispersed phase (W_1) suspended from a titanium mesh.

Beads	Emulsion used	UV Exposure	Pore size [μm]	Pore throat size [μm]	Surface pore throat size [μm]	Relative pore throat size ^a [%]	Porosity [%]	Enc. Eff. ^b [%]
TiDy-1	E12.5-60	5 min	7.4 ± 5.5	1.7 ± 0.6	1.9 ± 1.0	23%	79 ± 2	N/A
TiDy-2	E12.5-60 0.16M	2 min	6.4 ± 5.1	1.4 ± 0.5	1.9 ± 0.8	22%	79 ± 2	56%
TiDy-3	E12.5-60 0.16M	3 min	7.3 ± 7.0	1.7 ± 0.8	2.5 ± 1.1	23%	80 ± 2	58%
TiDy-4	E12.5-60 0.16M	4 min	7.7 ± 10.7	1.5 ± 0.7	1.8 ± 1.1	19%	77 ± 2	72%
^a Relative pore throat size was calculated as the ratio between average pore throat diameter and average pore diameter								
^b Encapsulation Efficiency								

The surface of beads TiDy-1, produced by polymerisation of emulsion templates E12.5-60 without HCl solution in the dispersed phase, was similar to a typical polyHIPE structure containing surface pore throats with an average size of $1.9 \pm 1.0 \mu\text{m}$ (Figure 7-10a). The internal morphology of the beads consisted of pores with an average pore size of $7.4 \pm 5.5 \mu\text{m}$, which were interconnected by pore throats with an average diameter of $1.7 \pm 0.6 \mu\text{m}$ (Figure 7-10b). Beads TiDy-2 were produced by polymerisation, which lasted for 2 min, of emulsion template droplets containing 0.16 M aq. HCl solution (E12.5-60 0.16M) in the dispersed phase (W_1) of the emulsion. The surface of beads TiDy-2 was also similar to a typical polyHIPE structure containing surface pore throats with an average size of $1.9 \pm 0.8 \mu\text{m}$ (Figure 7-10c), similar to beads TiDy-1. The internal pore structure of beads TiDy-2 was composed of pores with an average pore size of $6.4 \pm 5.1 \mu\text{m}$ interconnected by pore throats with an average size of 1.4 ± 0.5 (Figure 7-10d). The relative pore throat size of beads TiDy-2 was 22 %, again similar to previous beads TiDy-1 produced after polymerisation of emulsion templates without HCl in the dispersed phase of the emulsion. The similar relative pore throat size seems to indicate that the emulsion templates were stable during polymerisation. The encapsulation efficiency

of beads TiDy-2 was 56 % with a maximum amount of HCl that could be encapsulated in the beads of 181 $\mu\text{mol/g}$.

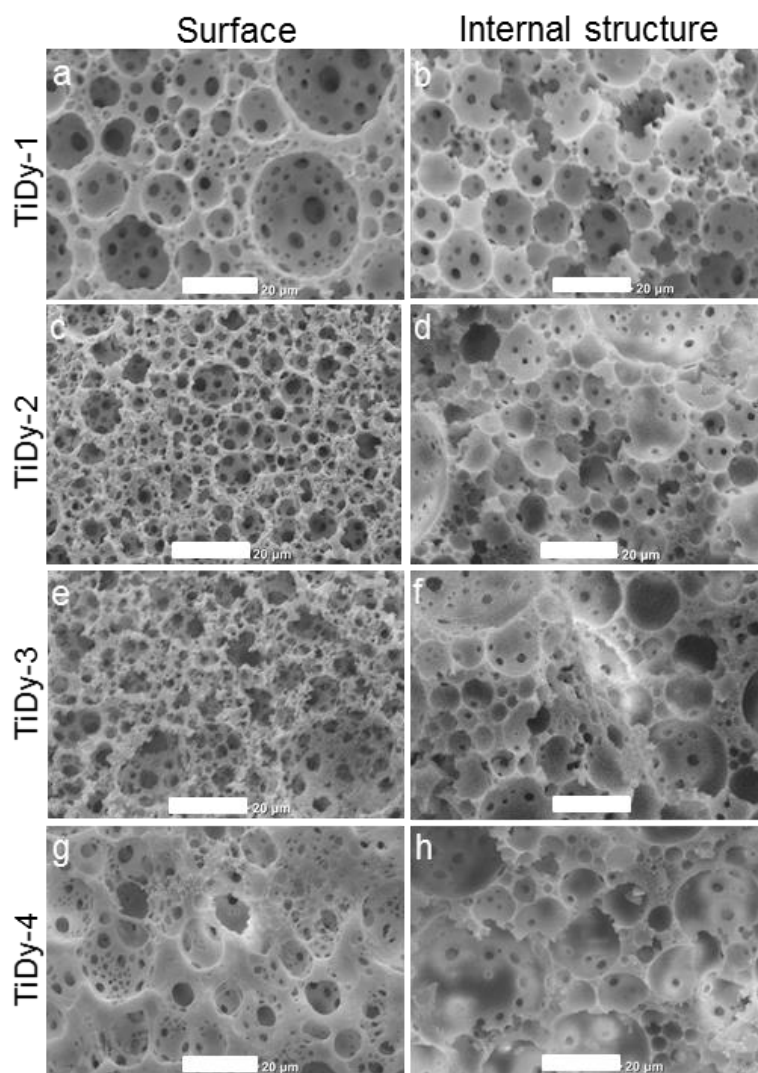


Figure 7-10. SEM images of the surface and internal pore structure of macroporous beads produced by polymerisation of emulsion templates with an internal phase volume ratio of 60 % stabilised with a surfactant concentration of 12.5 vol.%. Beads TiDy-2, 3 and 4 contained encapsulated HCl. All scale bars represent 20 μm .

It is worth mentioning that the maximum amount of HCl that could be encapsulated in macroporous polymer beads produced by polymerisation of the emulsion template (E12.5-60 0.16M) in our macrofluidic polymerisation device was 144 $\mu\text{mol/g}$ of beads, which represents an encapsulation efficiency of 49%. The increased encapsulation efficiency in beads produced by polymerisation of suspended droplets (it increased by $\sim 25\%$) compared to beads produced by macrofluidic polymerisation can be explained by the absence of the secondary aqueous

phase (W_2), which decreased the loss of HCl in the secondary aqueous phase due to diffusion. Beads TiDy-3, produced by UV irradiation of the emulsion droplets for 3 min, had a similar surface and internal morphology (Figure 7-10e and f) to beads TiDy-2, produced by 2 min polymerisation. In this case, the encapsulation efficiency was 58 % and the maximum amount of HCl encapsulated 185 $\mu\text{mol/g}$ of beads. Beads TiDy-4 produced after polymerisation of emulsion template droplets for 4 min had surface pore throats with an average size of $1.8 \pm 1.1 \mu\text{m}$ (Figure 7-10g). However, the surface of these beads also contained areas with a closed skinned surface as well. This kind of bead exterior could have been caused by partial destabilisation of the emulsion droplet surface during polymerisation. The formation of areas with a closed surface could help to explain the higher amount of HCl encapsulated, which was 230 $\mu\text{mol/g}$, representing an HCl encapsulation efficiency of 72 %. The internal pore structure of beads TiDy-4 contained pores with an average pore size of $7.7 \pm 10.7 \mu\text{m}$ interconnected by pore throats with an average size of $1.5 \pm 0.7 \mu\text{m}$ (Figure 7-10h). Beads TiDy-4 had the lowest porosity ($77 \pm 2 \%$) and relative pore throat size (19 %) of all beads produced, which contributed to higher retention of our model active ingredient in the internal pore structure of the beads.

Encapsulation of hydrochloric acid (HCl) in macroporous beads produced by polymerisation of multiple printed droplets and by sedimentation polymerisation using low and high intensity UV light sources

Using the UVC-8 Curing Conveyor System for more than 15 min resulted in an increase of the temperature inside the polymerisation unit due to the large amount of energy emitted in the infrared spectrum by the mercury lamp.³²⁰ During polymerisation of emulsion droplets by sedimentation or macrofluidic polymerisation, the presence of a secondary aqueous phase (W_2) combined with the rapid polymerisation of the emulsion droplets prevented loss of organic phase and HCl due to evaporation. Therefore, it is possible that macroporous beads produced by polymerisation of printed emulsion droplets in the UVC-8 Curing Conveyor System suffered a loss of encapsulated HCl by evaporation into the environment. In order to further increase the encapsulation efficiency, two other UV lights with limited emissions in the infrared spectrum were tested, namely a low intensity hand held UV light and a high-power UV LED. The influence of the UV source used to initiate the polymerisation of the emulsion template droplets on the surface and internal pore structure of macroporous beads produced

and the encapsulation efficiency was studied. A summary of the internal and surface morphology of the beads produced including average pore size, pore throat size and surface pore throat size of the beads, along with the encapsulation efficiency is presented in Table 7-7.

Table 7-7. Summary of the properties and encapsulation efficiency of beads obtained after polymerisation of the emulsion templates E12.5-60 containing different amounts of HCl as model active ingredient in the emulsion dispersed phase (W_1).

Beads	Polymerisation method	Pore size [μm]	Pore throat size [μm]	Surface pore throat size [μm]	Relative pore throat size ^a [%]	Porosity [%]	Encapsulation efficiency [%]
TiHH-1	Multidrop	4.7 ± 5.3	1.7 ± 0.8	2.4 ± 1.4	36%	73 ± 2	N/A
TiHH-2	Multidrop	5.5 ± 3.3	1.2 ± 0.5	1.7 ± 0.9	22%	77 ± 1	54%
TiHH-3	Multidrop	5.1 ± 3.7	1.3 ± 0.7	2.7 ± 1.2	25%	79 ± 2	91%
TiLED	Multidrop	7.3 ± 4.6	1.7 ± 0.6	1.9 ± 1.1	23%	80 ± 1	95%
SEHH-1	Sedimentation	9.8 ± 10.8	1.3 ± 0.5	3.4 ± 2.8	13%	77 ± 2	5%
SEHH-2	Sedimentation	5.3 ± 3.0	1.1 ± 0.3	2.0 ± 0.9	21%	77 ± 2	4%
^a Relative pore throat size was calculated as the ratio between average pore throat size and average pore size							

Beads TiHH-1, produced by polymerisation of emulsion templates (E12.5-60) without HCl in the dispersed phase of the emulsion for 60 min had an open pore surface similar to beads produced in the UVC-8 Curing Conveyor System but in this case the surface pore throats were slightly larger having an average diameter of $2.4 \pm 1.4 \mu\text{m}$ (Figure 7-11a1). These beads had an average pore size of $4.7 \pm 5.3 \mu\text{m}$ and interconnecting pore throats of $1.7 \pm 0.8 \mu\text{m}$ (Figure 7-11a2). The average pore size was higher than beads produced with the same formulation by polymerisation in the UVC-8 Curing Conveyor System ($7.4 \pm 5.5 \mu\text{m}$). The broader pore size seems to indicate a degree of emulsion destabilisation occurring during polymerisation, probably due to the longer polymerisation times required (60 min) compared to the photopolymerisation times required when using the UVC-8 Curing Conveyor System (less than 5 min). The surface of beads TiHH-2 were in part skinned, i.e. non-porous, but contained zones with surface pore throats with an average diameter of $1.7 \pm 0.9 \mu\text{m}$ (Figure 7-11b1). The surface of the beads was similar to that of the beads TiDy-4, produced after polymerisation of emulsion droplets having the same formulation (E12.5-60 0.16M) for 4 min using the UVC-8

Curing Conveyor System. The internal pore structure of beads TiHH-2 was composed of pores with an average diameter of $5.5 \pm 3.3 \mu\text{m}$ and pore throats of $1.2 \pm 0.5 \mu\text{m}$. The relative pore throat size of the beads TiHH-2 was 22 %, similar to that of the beads produced by polymerisation of emulsion template droplets with the same formulation using the UVC-8 Curing Conveyor System. This seems to indicate a limited influence of the UV light source used on the internal structure of the beads produced. The amount of HCl encapsulated determined by titration was $169 \mu\text{mol/g}$, reaching an encapsulation efficiency of 54 %, similar to beads TiDy-2 produced after polymerisation of emulsion droplets using the UVC-8 Curing Conveyor System for 2 min.

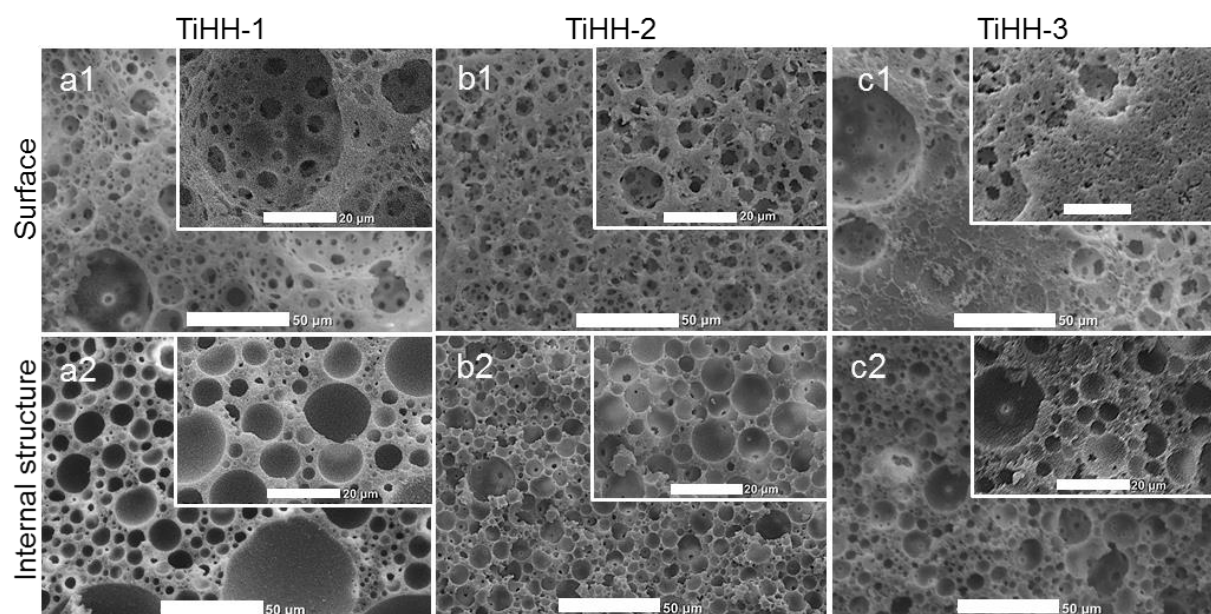


Figure 7-11. SEM images of beads TiHH produced by polymerisation of emulsion template droplets with an internal phase volume ratio of 60 % stabilised with a surfactant concentration of 12.5 vol.%. The emulsion droplets were suspended from a titanium mesh and polymerised using a hand-held UV light. Scale bars represent 50 μm and 20 μm in the inserts.

To produce beads TiHH-3, the UV irradiation time was increased from 40 to 60 min. Again, the surface of the beads produced had skinned, non-porous regions and zones containing surface pore throats with an average diameter of $2.7 \pm 1.2 \mu\text{m}$ (Figure 7-11c1). However, in this case the amount of surface pore throats was much lower. The internal structure of beads TiHH-3 was composed of pores with an average diameter of $5.1 \pm 3.7 \mu\text{m}$ and pore throats with an average size of $1.3 \pm 0.7 \mu\text{m}$ (Figure 7-11c2). The relative pore throat size was 25 %, similar to that of TiHH-2 beads, which were polymerised for 40 min. Surprisingly, the amount of HCl

encapsulated was 290 $\mu\text{mol/g}$, reaching an encapsulation efficiency of 91%. While no significant variations in the internal morphology of beads TiHH-2 and TiHH-3 can be observed, the much reduced number (but not average diameter) of the surface pore throats in the beads TiHH-3 could explain this drastic increase in encapsulation efficiency. Beads TiLED, produced by polymerisation of emulsion template droplets under a high-power UV LED for 4 min had surface pore throats with an average size of $1.9 \pm 1.1 \mu\text{m}$ (Figure 7-12a1). As for beads TiHH-3, a surface composed of open porous and skinned areas can be in SEM images. The internal pore structure was composed of pores with an average pore diameter of $7.3 \pm 4.6 \mu\text{m}$ interconnected by pore throats with an average size of $1.7 \pm 0.6 \mu\text{m}$, resulting in a relative pore throat size of 23%.

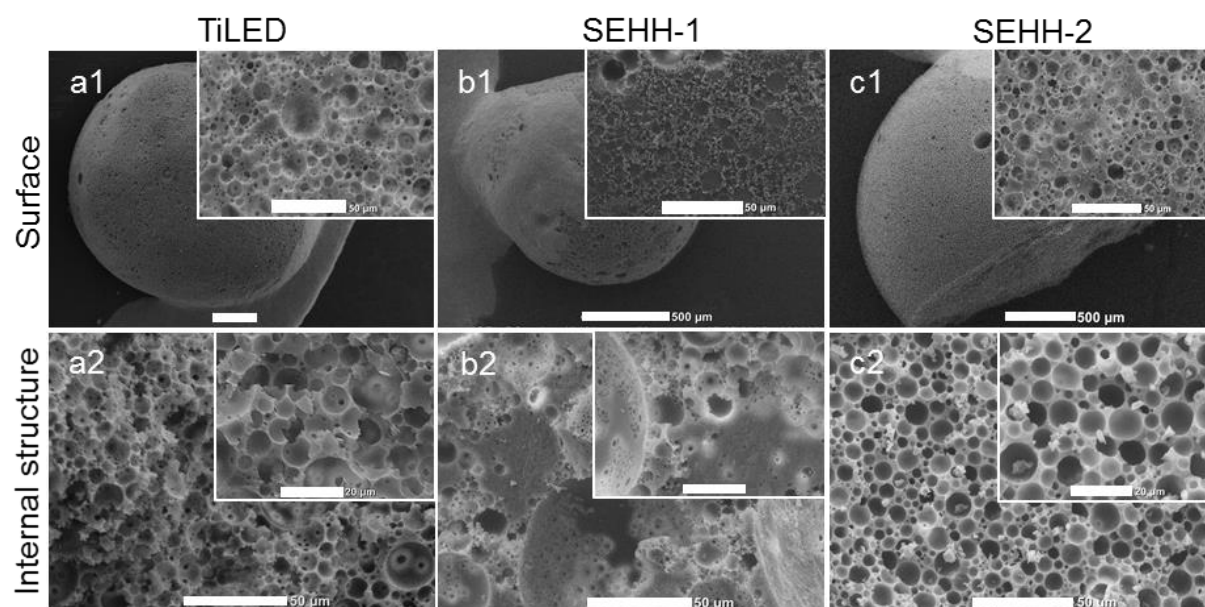


Figure 7-12. SEM Images of beads produced by polymerisation of emulsion templates containing with an internal phase volume ratio of 60 % stabilised with a surfactant concentration of 12.5 vol.%. The internal dispersed phase (W_1) consisted of a 0.16 M aq. HCl solution. Scale bars are 500 μm in a1, b1 and c1, and 50 μm in the inserts. Scale bar a2, b2 and c2 are 50 μm and 20 μm in the inserts.

The amount of HCl encapsulated in beads TiLED was even higher reaching 300 $\mu\text{mol/g}$, equivalent to an encapsulation efficiency of 95%. After comparing the surface and internal morphology of beads TiLED with other beads produced by polymerisation of printed suspended droplets, no dramatic variations were evident. The high encapsulation efficiency obtained can be explained by the combination of a rapid polymerisation and the fact that no secondary aqueous phase was needed, which dramatically reduced the loss of encapsulated HCl. Control beads SEHH-1 were produced by sedimentation polymerisation of emulsion

droplets containing a 0.16 M aq. HCl solution as dispersed phase (W_1) in distilled water (W_2). The bead surface consisted of areas with a closed surface and areas containing a few surface pore throats with an average diameter of $3.4 \pm 2.8 \mu\text{m}$ (Figure 7-12b1). The internal pore structure was composed of a mix of closed pores and pores containing pore throats with an average diameter of $1.3 \pm 0.5 \mu\text{m}$ (Figure 7-12b2). The average pore size was $9.8 \pm 10.8 \mu\text{m}$ but the beads also contained a few pores with a diameters of approximately $200 \mu\text{m}$, indicating some degree of emulsion destabilisation of the emulsion templates before polymerisation. This can be confirmed by the low relative pore throat size (13%) and the standard deviation of the average pore size. The encapsulation efficiency of beads SEHH-1 was only 5 %, indicating almost a complete loss of HCl into the secondary aqueous phase before or during polymerisation. It becomes evident that despite the fact that beads with an outer surface very similar to beads TiHH-3, comprising closed and open pore areas, the used of distilled water as secondary aqueous phase (W_2) combined with the longer polymerisation times required resulted in a poor encapsulation efficiency. With the intention to improve the encapsulation efficiency, beads SEHH-2 were synthesised using an aqueous solution containing 3 wt.% of PVA and Triton X-405 as secondary aqueous phase (W_2). In order to reduce diffusion of HCl from the dispersed phase (W_1) into the secondary aqueous phase (W_2), the polymerisation time was reduced from 60 to 40 min. The surface of beads SEHH-2 contained surface pore throats with an average size of $2.0 \pm 0.9 \mu\text{m}$, a reduction of 40 % compared with beads SEHH-1, which were produced in distilled water. Nevertheless, also in this case the encapsulation efficiency (of beads SEHH-2) was very low (4%). The surface of beads SEHH-2 and beads produced using the same formulation by macrofluidic polymerisation were compared (Figure 7-13). It can be noted that while the average size of the surface pore throats is similar ($1.4 \pm 0.8 \mu\text{m}$ and $2.0 \pm 0.9 \mu\text{m}$), surface pore throats in beads produced by macrofluidic polymerisation were less frequent (Figure 7-13b1). The differences in surface morphology but mainly the longer polymerisation times required to solidify the emulsion droplets explain the dramatic reduction in encapsulation efficiency of beads produced by sedimentation polymerisation (from 49 to 4 %).

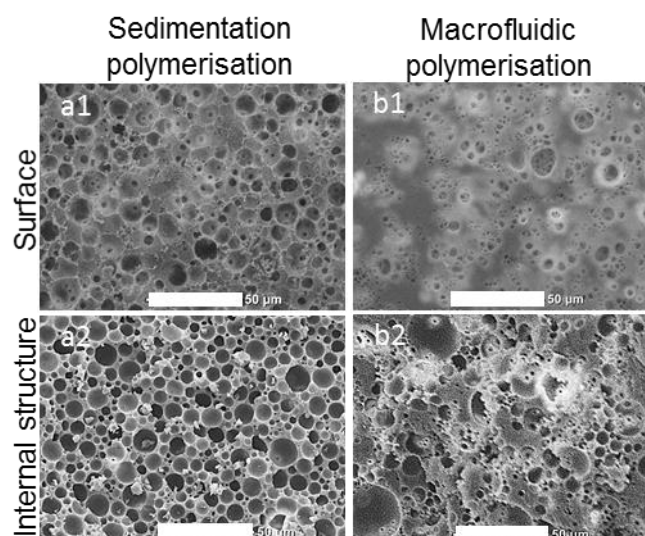


Figure 7-13. SEM images of the surface and internal pore structure of beads produced by sedimentation and macrofluidic polymerisation of emulsion templates containing a 0.16 M aq. HCl solution as dispersed phase (W_1).

The relative pore throat diameter of beads SEHH-2 was 21 %, with a porosity of approximately 77 %. Beads produced by macrofluidic polymerisation had a relative pore throat size of 24 % and a porosity of 70 % supporting the hypothesis that the loss of active ingredient is not due to a dramatic change in bead morphology but due to longer polymerisation times required when using the low intensity hand held UV light and, therefore, longer residence times in distilled water, before solid macroporous beads were produced.

7.4 Summary

The aim was explore alternatives to increase the encapsulation efficiency of active ingredients in macroporous beads produced by polymerisation of W_1/O emulsion templates. Semi-spherical beads were produced by polymerisation of printed emulsion template droplets with an internal phase volume ratio of 60% stabilised with a surfactant concentration of 12.5 vol.%. A 0.16 M aq. HCl solution was used as emulsion dispersed phase (W_1). Beads were produced by photopolymerisation of printed emulsion droplets suspended from a titanium mesh using the high power UVC-8 Curing Conveyor System (Beads TiDy). These beads had an encapsulation efficiency between 56 and 72 %. In this case no secondary aqueous phase (W_2) was needed, which resulted in a dramatic increase of the encapsulation efficiency, the relatively high temperatures (between 40 and 60°C) inside the UVC-8 Curing Conveyor System might have negatively affected the encapsulation efficiency.

Beads TiHH and TiLED produced by polymerisation of printed emulsion template droplets suspended from a titanium mesh using a low intensity hand held UV light and a high power UV LED reached encapsulation efficiency exceeding 90%. While the production yield was not measured, no shrinking of the emulsion droplets during polymerisation was observed by the naked eye. However, the high porosities observed (~80%) indicated a loss of organic phase during polymerisation.

Beads produced by macrofluidic polymerisation using emulsion templates with the same formulation had an encapsulation efficiency of 49% (see Chapter 6). The evidence analysed so far supports the idea that high encapsulation efficiencies are restricted not only by the bead morphology but mainly by loss of the model active ingredient HCl into the secondary aqueous phase (W_2) by diffusion through the oil phase prior to polymerisation of the emulsion template. The poor encapsulation efficiency of HCl in macroporous beads (4 %) produced by sedimentation polymerisation of emulsion droplets in an aqueous solution containing 3 wt.% of PVA and Triton X-405 as secondary aqueous phase (W_2) also support this hypothesis.

Chapter 8. Overall conclusions and recommendations for future work

8.1 Overall conclusions

The production of macroporous polymer beads by polymerisation W_1 /MMA-EGDMA emulsion template droplets with aim to use them as delivery systems for active ingredients was investigated. First, emulsions were formulated to produce emulsion templates which after polymerisation of the minority yet continuous monomer emulsion phase lead to macroporous polymer beads with a closed surface or internal pore structure and, therefore, a higher encapsulation efficiency. The internal phase volume ratio and surfactant concentration used to stabilise the emulsion templates was varied to determine the boundaries between close celled beads and beads with an interconnected pore structure. Beads with a close celled pore structure were produced by sedimentation polymerisation of emulsion templates stabilised with a surfactant concentration between 5 and 10 vol.%. Furthermore, additives in the secondary, external aqueous phase (W_2) were investigated to create macroporous polymer beads with a dense bead surface layer. It was also attempted to vary the locus of initiation to produce beads with a closed celled pore structure. The beads produced by using photoinitiator in the dispersed and continuous phase of the emulsion template droplets and PVA and Triton X-405 in the secondary aqueous phase (W_2) had a reduced interconnectivity. In this case, macroporous beads with a few surface pore throats with a diameter of $1.7 \pm 1.1 \mu\text{m}$ and interconnecting pore throats with an average size of $0.4 \pm 0.1 \mu\text{m}$ were obtained, the smallest of all formulations tested.

The production of large quantities of millimetre sized porous beads by polymerisation of emulsion templates faced two mayor challenges; i) the poor control over size dispersion in case of suspension polymerisation and ii) the low production rates in case of microfluidic polymerisation. A lab scale continuous plug-flow reactor for the production of macroporous beads with an average size between 200 – 1000 μm by UV photopolymerisation of H/MIPE template droplets was designed, built and tested. Using this reactor it was possible to control the size distribution of the beads. The bead size was controlled by varying the (W_1 /O) emulsion injection and recirculating carrier phase (W_2) velocity. The coefficient of variation in bead size

of the beads produced using the macrofluidic plug-flow reactor was in the order of 20%. The maximum rate achieved using this setup was 54 mL of beads/h avoiding.

Additionally, macroporous beads (and monoliths) containing encapsulated HCl were produced by polymerisation of emulsion templates containing aqueous HCl as dispersed phase (W_1). The use of a secondary aqueous phase (W_2) containing PVA and Triton X-405 resulted in an increased encapsulation efficiency of the beads produced. For example, after injection and polymerisation of emulsion droplets containing a 0.16 M aqueous HCl solution as dispersed phase, beads with a maximum amount of encapsulated HCl of 144 $\mu\text{mol/g}$ could be produced. In this case, the encapsulation efficiency increased from 19% to 49 %.

In order to further increase the production versatility of macroporous polymer beads a technique inspired by the multi-drop process commonly used for the industrial production of biscuits and meringues was adapted to produce such beads by printing and subsequent polymerisation of emulsion template droplets suspended from a titanium mesh. In order to demonstrate the principle a modified desktop 3D printer was used to produce beads by photopolymerisation of emulsion template droplets using a low intensity hand held UV light or a high-power UV LED pen, achieving encapsulation efficiencies of 90 and 95%, respectively.

8.1 Recommendations for future work

Despite four years of research some challenges still need to be considered in future research in order to produce beads that can be used as effective delivery systems. It was noted that the outer skin of the beads produced still contained several pores, which decreased the retention of encapsulated HCl in the internal pore structure of the beads during storage. An improved retention of the active ingredient in macroporous beads produced by emulsion templating could be achieved by:

- Initiating the polymerisation from the internal dispersed emulsion phase and secondary carrier phase simultaneously.
- Using redox initiators in the dispersed phase (W_1) of the emulsion could result in beads with a close celled morphology. A similar approach was already used to produce monoliths with a close celled internal pore structure after polymerisation.²⁹⁶
- The use of compounds with a low vapour pressure as active ingredients would also aid the retention of an encapsulated ingredient over time or at least reduce the rate of loss.

The macrofluidic plug-flow reactor designed could be easily scaled up to further increase the production rates of macroporous polymer beads. It is worth mentioning that using a recirculating carrier phase in the plug flow reactor allows for an easy modification and control of the composition and other synthesis parameters, i.e temperature of the secondary aqueous phase (W_2).

The use of different solvents in the organic phase of (W_1/O) emulsion droplets often led to the formation of a dense surface layer after polymerisation in a secondary aqueous phase (W_2).³²¹ This effect could be used to enhance the encapsulation and retention potential of macroporous beads obtained by polymerisation of multiple emulsion templates. However, interactions between solvent and encapsulated active ingredient should be taken into account. For example, bacteria could be encapsulated, which could be used for the degradation of multiple-ring aromatic hydrocarbons present in waste water of fracking fluids.³²² However, the use of emulsion templates containing solvents could be incompatible with the encapsulated microorganisms.

The use of production setups based on a recirculating carrier phase, such as our plug flow macrofluidic reactor, allows for easy control or modification of the carrier phase composition. As the macrofluidic plug-flow reactor can be easily scaled up, this could be used as an environmentally friendlier alternative to obtain large amounts of macroporous beads with a closed surface without the need of solvents. Additionally, it is possible to optimise the active ingredient concentration gradient if the active ingredient to encapsulate present in the dispersed phase of the emulsion droplets and is also dissolved in the recirculating carrier phase which should result in an increased encapsulation efficiency.

Pickering emulsion templates could be used to produce macroporous beads with a close celled pore structure. This particular morphology may result in high encapsulation efficiencies and the retention of the encapsulated ingredients for longer periods of time. However, Pickering emulsions tend to have high viscosities and the drag forces produced during co-flow injection into an aqueous carrier phase not be sufficient to “cut” the emulsion from the injector system and to form individual droplets which might result in non-spherical beads or filaments after

polymerisation. This problem could be partially prevented by increasing the viscosity of the carrier phase used in the macrofluidic plug flow reactor, e.g. by adding high molecular weight polymers to the carrier phase.

The use of multi-drop polymerisation offers an alternative for the production of macroporous beads by polymerisation of highly viscous emulsion templates. The main drawback of the current lab based setup are the extremely low production rates obtained (one bead every 4.5 min). The production rates could be increased by using a combination of several dispense and polymerisation heads or by printing droplets directly onto the conveyor belt of the UV-curing system.

Appendix – Support Information

A-1 Support information Chapter 2

Equations developed by Oldroyd for the calculation of relative viscosity:

$$\left(1 + \tau_1 \frac{D}{Dt}\right) \bar{\tau} = 2\eta_0 \left(1 + \tau_2 \frac{D}{Dt}\right) \bar{E} \quad \text{Equation A2-13}$$

where $\bar{\tau}$ is deviatoric stress tensor, η_0 is the zero-shear viscosity of emulsion, τ_1 is a relaxation time, and τ_2 is a retardation time and $\frac{D}{Dt}$ is the Jaumann derivative.

Equations for the calculation of η_0 , the zero-shear viscosity of emulsion, τ_1 and τ_2 , the relaxation time and retardation time respectively.

$$\eta_0 = \eta_c \left[\frac{10(1 + \lambda) + 3\phi(2 + 5\lambda)}{10(1 + \lambda) - 2\phi(2 + 5\lambda)} \right] \quad \text{Equation A2-14}$$

$$\tau_1 = \left(\frac{\eta_c R}{4\gamma} \right) \left[\frac{(2\lambda + 3) + 2\phi(1 + \lambda)}{10(\lambda + 1) - 2\phi(2 + 5\lambda)} \right] (16 + 19\lambda) \quad \text{Equation A2-15}$$

$$\tau_2 = \left(\frac{\eta_c R}{4\gamma} \right) \left[\frac{(2\lambda + 3) - 3\phi(1 + \lambda)}{10(\lambda + 1) - 2\phi(2 + 5\lambda)} \right] (16 + 19\lambda) \quad \text{Equation A2-16}$$

where λ is the viscosity ratio η_d/η_c and R is the droplet radius.

Terms of the mathematical model developed by Pal (Equation 2-1) to describe the viscoelastic properties of emulsions with an internal phase volume ratio below 0.64. ($0 \leq \phi \leq 0.64$). The effective volume fraction $\psi\phi$ is represented by Equation A2-5:

$$\psi\phi = 1 - \exp \left[\frac{-\phi}{1 - (\phi/\phi_{max})} \right] \quad \text{Equation A2-17}$$

where ϕ_{max} is the maximum packing volume of non-deformable droplets, which for random close packing of spherical particles is about 0.64.

The term H^* of Equation 2-4 is presented below in Equation A2-6:

$$H^* = \frac{(G_d^*(\omega) - G_c^*(\omega))(19G_d^*(\omega) + 16G_c^*(\omega)) + (4\gamma/R)(5G_d^*(\omega) + 2G_c^*(\omega))}{(2G_d^*(\omega) + 3G_c^*(\omega))(19G_d^*(\omega) + 16G_c^*(\omega)) + (40\gamma/R)(G_d^*(\omega) + G_c^*(\omega))} \quad \text{Equation A2-18}$$

where G_d^* and G_c^* are the complex shear modulus of the dispersed and continuous phase respectively, R is the droplet radius and γ represents the interfacial tension.

Model developed by Princen for model emulsions of high internal phase volume ratio to represent the relation of yield stress (τ_0) and the static shear modulus (G):

$$\tau_0 = 1.05 \frac{\gamma \cos \theta}{R} \phi^{1/2} F \quad \text{Equation A2-19}$$

$$G = 0.525 \frac{\gamma \cos \theta}{R} \phi^{1/2} \quad \text{Equation A2-20}$$

where γ is the interfacial tension, θ the contact angle associated with the thin films separating adjacent droplets, R the radius of droplets and ϕ the volume fraction of the dispersed-phase.

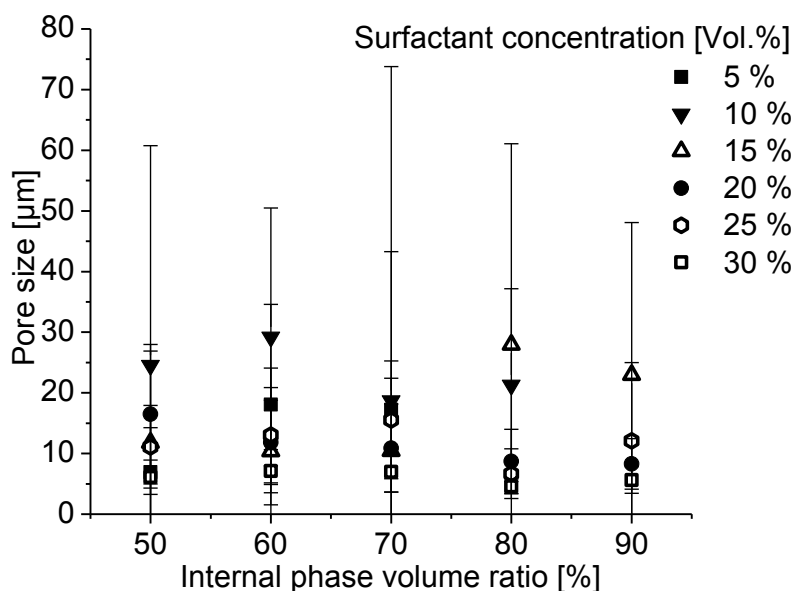
A-2 Support information Chapter 4

This section contains complementary information about the morphology of macroporous beads synthesised via sedimentation polymerisation

Table A2-1. Pore size of beads obtained from emulsion templates with different internal phase volume ratios and stabilised with increasing surfactant concentrations.

Surfactant concentration [vol%]	Pore size [μm]				
	50	60	70	80	90
30	6.1 ± 2.8	7.1 ± 3.5	6.9 ± 3.3	4.6 ± 1.2	5.62 ± 2.2
25	11.1 ± 6.8	13 ± 7.9	15.6 ± 9.7	6.7 ± 4.1	12.1 ± 12.9
20	16.5 ± 11.5	11.8 ± 6.9	10.9 ± 7.3	8.7 ± 5.3	8.3 ± 4.2
15	11.8 ± 15.2	10.4 ± 13.7	10.4 ± 12	27.9 ± 33.1	22.9 ± 25.2
10	24.6 ± 36.2	16.6 ± 17.2	18.7 ± 55.1	21.3 ± 15.9	
5	6.9 ± 7.3	18.1 ± 16.5	17.2 ± 26.1	No emulsion formed	

Figure A2-1. Pore size of beads obtained from emulsion templates with different internal phase volume ratios and stabilised with increasing surfactant concentrations.



After analysing the average pore size in beads produced by polymerisation of emulsion templates with increasing internal phase volume ratios, no significant trend could be observed.

Table A2-2. Pore throat size of beads obtained from emulsion templates with different internal phase volume ratios and stabilised with increasing surfactant concentrations. The use of surfactant concentrations below 5 vol.% led to the formation of beads with closed pores.

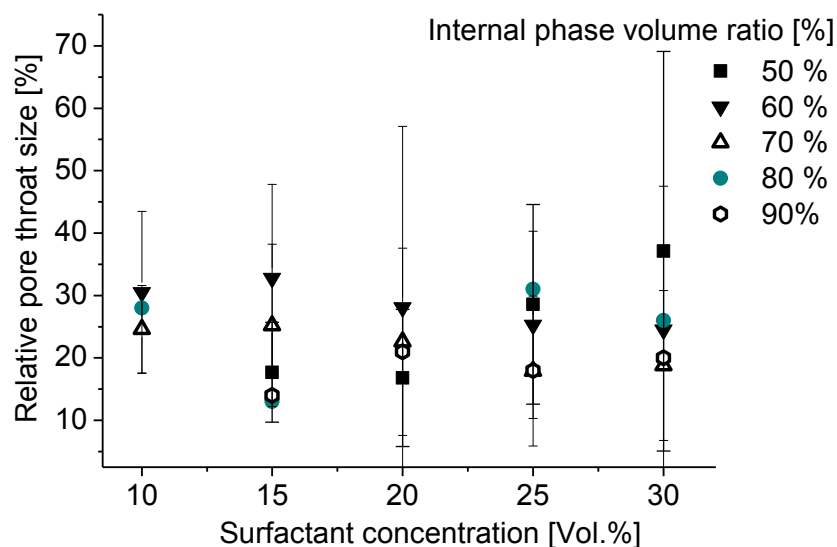
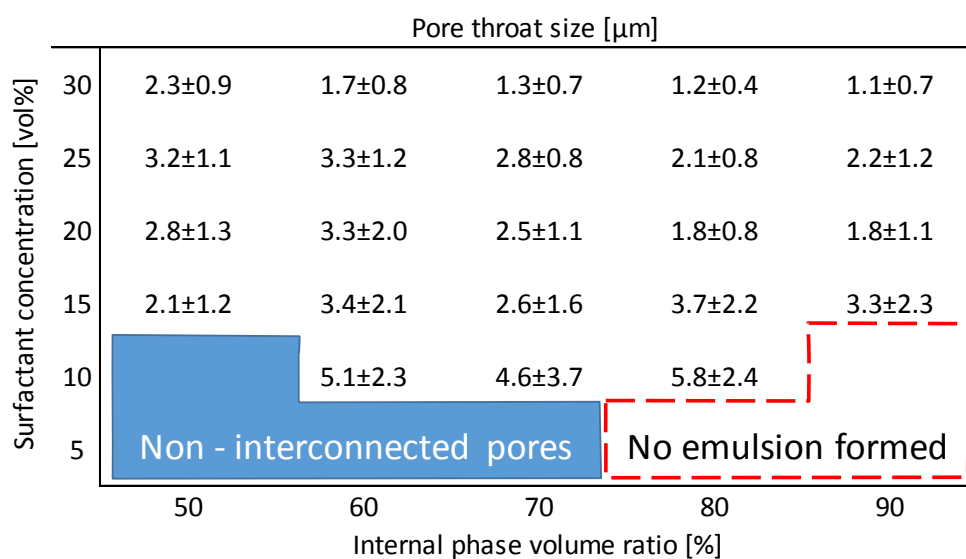


Figure A2-2. Relative pore throat size of beads produced by polymerisation of emulsion templates with different internal phase volume ratios and stabilised with increasing surfactant concentrations.

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