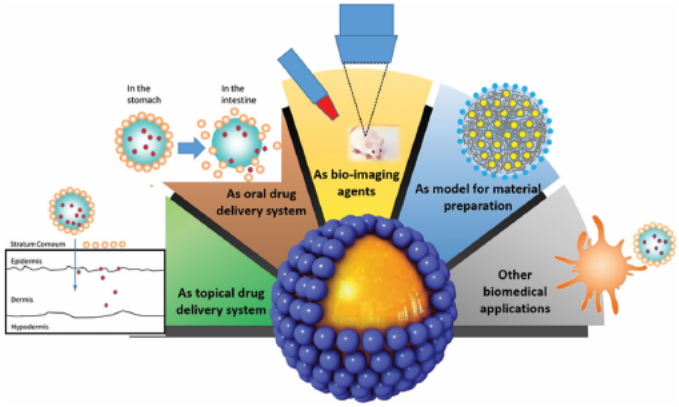
Recent Studies of Pickering Emulsions: Particles Make the Difference

*Jie Wu and Guang-Hui Ma**



From the Contents

In recent years, emulsions stabilized by micro- or nanoparticles (known as Pickering emulsions) have attracted much attention. Micro- or nanoparticles, as the main components of the emulsion, play a key role in the preparation and application of Pickering emulsions. The existence of particles at the interface between the oil and aqueous phases affects not only the preparation, but also the properties of Pickering emulsions, affording superior stability, low toxicity, and stimuli-responsiveness compared to classical emulsions stabilized by surfactants. These advantages of Pickering emulsions make them attractive, especially in biomedicine. In this review, the effects of the characteristics of micro- and nanoparticles on the preparation and properties of Pickering emulsions are introduced. In particular, the preparation methods of Pickering emulsions, especially uniform-sized emulsions, are listed. Uniform Pickering emulsions are convenient for both mechanistic research and applications. Furthermore, some biomedical applications of Pickering emulsions are discussed and the problems hindering their clinical application are identified.

1. Introduction

Emulsions and materials prepared using emulsions as templates have been widely explored in the biomedical field as drug carriers and tissue engineering materials, among other things. Due to the high interfacial area of the dispersed droplets, emulsions without emulsifiers are thermodynamically unstable systems. In order to stabilize the emulsion droplets, low molar mass surfactants or surface-active polymers usually have to be included in the formulations to decrease the interfacial tension between the phases. Studies carried out by Ramsden and Pickering revealed another way of stabilizing the droplets, i.e., by using solid particles (usually nano- or microscale) to replace the surfactants.[1,2] However, the particle-stabilized emulsions (known as Pickering emulsions) did not attract much attention until a decade ago. With the rapid development of materials science, which provided numerous alternative particles, researchers recognized that the use of particles as emulsion stabilizers could allow more varied designs. Moreover, Pickering emulsions possess many unique features that classical emulsions stabilized by surfactants do not, such as superior stability and low toxicity.

Many researchers conducted extensive, systematic work on Pickering emulsions, such as the groups led by Prof. B. P. Binks at the University of Hull, Prof. A. D. Dinsmore at Harvard University, Prof. M. Mass at the University of Bremen, Prof. K. Nagayama at JRDC, and Prof. T. Ngai at the Chinese University of Hong Kong. In addition, they also used Pickering emulsions as templates for the preparation of microcapsules with colloidal particle shells (known as colloidosomes), materials with porous structures or stimuli-responsiveness, which enriches and expands the application of Pickering emulsions.[3–6] Several reviews on various aspects of the development of Pickering emulsions have been published, such as reviews on emulsions prepared by biomass-based particles[7,8] and stimuli-responsive Pickering emulsions,[9,10] along with some examples of applications of Pickering emulsions in different fields.[11,12] Two professional books comprehensively dealing with the background, research status, and developing trends of Pickering emulsions have been published, and it is strongly recommended that researchers consult them.[13,14]

In recent years, the rapid development of materials technology has increased the variety of particles available. The effect of the inherent properties of the particles on the preparation, characteristics, and applications of Pickering emulsions is not negligible, and thus it is necessary to review this aspect. Moreover, because of the progress in the development of Pickering emulsions, the range of fields in which they can be applied has broadened. More and more papers related to biomedical applications of Pickering emulsions are being published.

As a promising material for biomedical applications, Pickering emulsions possess well-defined properties, including superior stability, adjustable permeability, better biocompatibility without the addition of surfactants, etc. Moreover, the versatility of Pickering emulsions enables a diversity of functionalities to meet the various needs of application. Based on recent research, several promising Pickering emulsion-based formulations that have high potential as drug delivery systems or imaging agents with outstanding performance have been proposed.

This article aims to provide an up-to-date review on Pickering emulsions and their potential biomedical applications. The effect of particles on the preparation and properties of Pickering emulsions as well as some recent studies related to the preparation of uniform-sized Pickering emulsions will be introduced in this review. Although Pickering emulsions have been academically investigated for many years, they are not yet present in any commercial formulations used for human biomedicine. The main obstacles to its application may be a lack of understanding of its mechanism of action, its metabolism, and other safety issues. Hence, the challenges that need to be overcome before their practical application is possible will be highlighted. For biomedical applications of Pickering emulsions, two aspects will be introduced in this manuscript, viz. the direct use of Pickering emulsions as a topical and oral drug delivery system and the application of Pickering emulsions as templates to prepare materials that can be used in biomedical applications.

2. The Effect of Particles on the Preparation of Pickering Emulsions

2.1. Wettability of Particles

Since Pickering emulsions were first reported a century ago, their stabilization mechanism has been investigated intensively. The driving force for the assembly of particles at the interface between two phases is the reduction of the interfacial area. Most research has concluded that in order to obtain stable Pickering emulsions, the key factor is particle wettability, which can be characterized by the contact angle θ at the oil–particle-water interface, as shown in **Figure 1**.[15]

For hydrophilic particles with $\theta < 90°$, the majority of particles would immerse in the aqueous phase, inducing the formation of an oil-in-water (o/w) emulsion. In order to obtain water-in-oil (w/o) emulsions, hydrophobic particles with $\theta > 90°$ should be used. Particles with an angle of 90° at the oil-water interface possess the maximum desorption energy, E, as calculated by Equation (1).[16]

$$E = \pi R^2 \gamma_{ow} (1 + \cos\theta)^2 \quad (1)$$

In Equation (1), γ_{ow} represents the tension of the interface and R represents the radius of a single spherical particle.

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In earlier work, surfactants were used with particles as emulsifiers to obtain the desired contact angle.[17,18] Emulsion systems with surfactants are unsuitable for studying the stabilization mechanism of Pickering emulsions. The research group led by Binks systematically studied the stabilization mechanism of particle-stabilized emulsions in the absence of surfactant molecules by using particles with different hydrophobicities in a range of oil-water systems.[16,19,20] For example, they investigated the effect of the wettability of SiO_2 nanoparticles on the stability of a toluene-water system.[16] The wettability of SiO_2 particles was altered by silanization on their surface. The emulsions made using very hydrophilic or very hydrophobic particles were unstable and coalesced. Only particles with intermediate hydrophobicities ($\theta \approx 90°$) could readily accumulate at the oil–water interface and stabilize the emulsions.

Moreover, the homogeneity of the surface wettability also affects the performance of particles when stabilizing emulsions. A representative example is the Janus particle, having two surfaces with opposing wettabilities, which can strongly attach to the oil–water interface and provide better emulsion stability. Based on a theoretical study of the thermodynamics of emulsion stabilization using amphiphilic Janus dumbbells, Lee et al. proved the existence of a lowest energy state of emulsions when the surfaces of the droplets were completely covered by Janus dumbbells.[21] Due to their high emulsion stabilizing capability, the number of reports on Pickering emulsions with Janus particles as emulsifiers has increased in recent years, and several novel materials based on these Pickering emulsions have been developed.[22,23]

Due to the importance of particle wettability for the preparation of Pickering emulsions, methods of accurately measuring the wettability have been explored by several works.[24–26] For example, one technique measures the time taken for a particle with a known volume to sink from the air-fluid interface to the bottom, to investigate how particle wettability affects its flotation characteristics. However, since many other properties, such as density and size, might also affect the flotation characteristics, different types of particles cannot be compared. Harwell et al. compared multiple techniques for characterizing the wettability of silica nanoparticles with different hydrophobicities[27] and found that measuring the heat of immersion by microcalorimetry was the best method for discriminating the difference in the wettabilities of particles.

2.2. Size of Particles

It can be concluded from Equation (1) that besides the wettability, the size of particles also has a profound effect on their desorption energy. Binks et al. used monodisperse hydrophobic latex particles of different average sizes to study the effect of particle size on the properties of the prepared emulsions.[28] They found that the sedimentation stability of the emulsions, characterized by the ratio of separated oil to the total oil volume, decreased on increasing the particle diameter in the 0.21 to 2.7 μm range.

All emulsions were stable against coalescence for more than 6 months and the diameters of the emulsion droplets formed initially increased with increasing particle diameter, and then remained constant. Using a membrane emulsification technique that allowed the preparation of uniform particles of different average sizes, Nan et al. fabricated uniform chitosan-coated alginate particles of three sizes (230 nm, 550 nm, and 1100 nm) to prepare Pickering emulsions.[29] According to Equation (2), the concentration of particles required to stabilize the droplets is proportional to their average diameter (r_p), and the experiment proved this result.

$$m_p = (16/3)\pi r_p \rho_p r_e^2 n_e \quad (2)$$

In Equation (2), r_e represents the radius of the emulsion droplet, n_e is the number of droplets in the emulsion, m_p is the mass of the particles, and ρ_p represents the density of the particles.

The size of the particles also affects the stabilization mechanism of Pickering emulsions. Qi et al. found that using small poly(D,L-lactic-co-glycolic acid) (PLGA) particles (330 nm) allowed the formation of dense layers arranged at the droplet interface, which prevented droplet coalescence and lowered the interfacial tension more effectively than when using two other particle sizes (620 nm and 1150 nm).[30] Moreover, the adsorption kinetics of the larger particles were slow and resulted in high adsorption barriers and less efficient packing at the interface.

2.3. Shape of Particles

In early work, most of the particles used in Pickering emulsions were spherical. In recent years, with ever-growing

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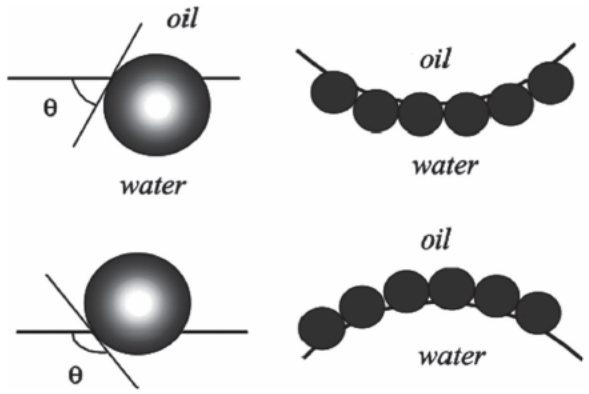

Figure 1. Contact angle (left) and corresponding probable positioning (right) of spherical particles at the oil-water interface. Reproduced with permission.[15] Copyright 2002, Elsevier.

research into the preparation of non-spherical particles, the emulsion stabilization efficiencies of particles with different shapes, including rods, fibers, and cubes, have also been investigated, as listed in **Table 1**.

Madivala et al. studied the effects different particle shapes on emulsion stability.[37] They prepared elliptical polystyrene (PS) particles via stretching and used them as stabilizers for Pickering emulsions. At higher concentrations, the particles at the interface connected end to end to form a triangular mesh structure, which constituted the skeleton of the emulsion and inhibited droplet coalescence. Furthermore, at lower concentrations the particles formed striped structures. When compared with spherical particles, elliptical particles were found to stabilize emulsions more effectively, and the stability increased as the aspect ratio of the particles increased.[38] Kalashnikova et al. prepared cellulose nanorods with aspect ratios between 13:1 and 160:1, and used these particles to prepare Pickering emulsions.[39] Because these nanorods connected together and formed bridge structures at the interface, super-stable Pickering emulsions were obtained.

2.4. Surface Properties of Particles

Particles with large surface areas tend to aggregate in solution. In order to keep a particle dispersion stable, there must be some steric hindrance or electrostatic repulsion between the particles. However, the force between the particles will hinder their adsorption onto the interface, which is known as the activation barrier for particle adsorption. Frechette et al. used ion-pair gold nanoparticles to investigate the effect of electrostatic force on the reversible adsorption of particles at the oil-water interface and on the assembly of adsorbed particles.[40] By increasing the pH of the aqueous solution, the desorption of particles from the interface can be achieved due to the increase in electrostatic repulsion between the particles. Other studies also showed that the electrostatic force would affect the adsorption of particles at the oil-water interface, the assembly separation of particles on the interface, and the stability of the formed Pickering emulsions.[41–43] Klumperman et al. studied the effect of the surface concentration of graft on the stability of Pickering emulsions.[44,45] They established a theoretical model and calculated a suitable surface concentration of graft for particles to achieve both the partial wetting and colloidal stability that are necessary for preparing stable Pickering emulsions. Subsequently, they experimentally verified the feasibility of their theoretical results. However, they also pointed out that the major limitation of the theoretical model was that it did not account for the curvature of the w/o interface, which would affect the packing and interactions of the particles at the w/o interface. Harwell et al. also found that the fraction of the surface covered by silane groups would affect the structure of the emulsion more profoundly than the contact angles of the particles.[27] Besides the surface graft concentration, other surface properties of particles also affect the stability of Pickering emulsions. For example, the surface roughness of the particles would reduce their contact surface, decrease the interfacial potential, and negatively affect the stability of the emulsions.[46] However, the opposite phenomenon has also been observed.[47] At present, the amount of related literature is not enough to establish the affecting law, and the range of research objectives also needs to be broadened.

2.5. Concentration of Particles

To evaluate the stability of droplets, regardless of whether they are stabilized by particles or surfactants, one key parameter, the capillary number, has been widely adopted and can be calculated according to Equation (3).[48]

$$Ca = (U\eta_c)/\sigma_{12} = (\varepsilon^{\bullet} R\eta_c)/\sigma_{12} \quad (3)$$

In Equation (3), U is the velocity, η_c is the viscosity of the continuous phase, σ_{12} is the interfacial tension between the

Table 1. Some examples of Pickering emulsions stabilized by non-spherical particles.

Type of particles	Particle shape	Oil phase	Aqueous phase	Type of emulsions	Reference
Hydroxyapatite nanoparticles	Sphere, rod, fiber	Methyl myristate	Milli-Q water	o/w	[31]
Halloysite nanotubes	Nanotube	Dichloromethane	water	o/w	[32]
Poly(lauryl methacrylate)$_{16}$ – benzyl methacrylate$_{37}$ nanoparticles	worm	n-dodecane	water	w/o	[33]
Hexagonal α-zirconium phosphate nanodisks	disk	dodecane	DI water	o/w	[34]
Hematite (α-Fe_2O_3) microparticles	Cube, ellipsoid, peanut	decane	Millipore water	o/w	[35]
Poly(methyl methacrylate)/poly(styrene-2-(2-bromoisobutyryloxy)ethyl methacrylate)-graft-poly(2-(dimethyl amino)ethyl methacrylate)	Mushroom	1-octanol	water	o/w	[36]

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two phases, $\dot{\varepsilon}$ is the extension rate, and R is the maximum size of the formed stable drops.

When the capillary number reaches a critical value, the formed droplets will break up. As shown in Equation (3), the capillary number is proportional to the size of the droplets. Thus, in order to preserve the emulsion stability, small droplets are more favorable. It has been proved that when using surfactants to stabilize emulsions, as the surfactant concentration increases, the size of the droplets decreases and the emulsion stability is improved. When the concentration of the surfactants reaches the critical micelle concentration, the droplet size remains constant.

For most Pickering emulsion systems, the increase in particle concentration not only decreases the formed droplet size and improves surface coverage, but also leads to the formation of a network structure around the emulsion droplets, which further improves the emulsion stability.

Binks et al. studied the influence of SiO_2 particle concentration on the droplet size of an o/w emulsion system.[3] They found that at low particle concentrations (lower than 3%), the droplet size of the emulsion would decrease with increasing particle concentration. A 10-fold increase in particle concentration reduced the droplet size to about 1/8 of the original. When the concentration of particles was higher than 3%, the droplet size would not change with the increase in particle concentration, and the extra particles tended to disperse in the continuous phase, not adsorb at the droplet interface. Arditty et al. found that if the particle concentration was low, the emulsion droplet surface could not be covered completely and coalescence occurred.[49] On increasing the particle concentration, the emulsion stability was enhanced.

On the other hand, some studies showed that under certain conditions, a high surface coverage of the emulsion droplets was not necessary for obtaining stable emulsions. Midomre et al. used SiO_2 particles and hydroxypropyl cellulose together as emulsion stabilizers.[50] They found that in order to achieve a stable emulsion, the surface coverage could be as low as 29%. Vignati et al. studied the Pickering emulsion stabilization mechanism at low surface coverage using microscopy.[46] They observed that when the surface coverage was low, the emulsion droplets approached each other, and the particles attached to the droplet surface would redistribute in the contact region between the droplets and inhibit coalescence, as shown in **Figure 2**.

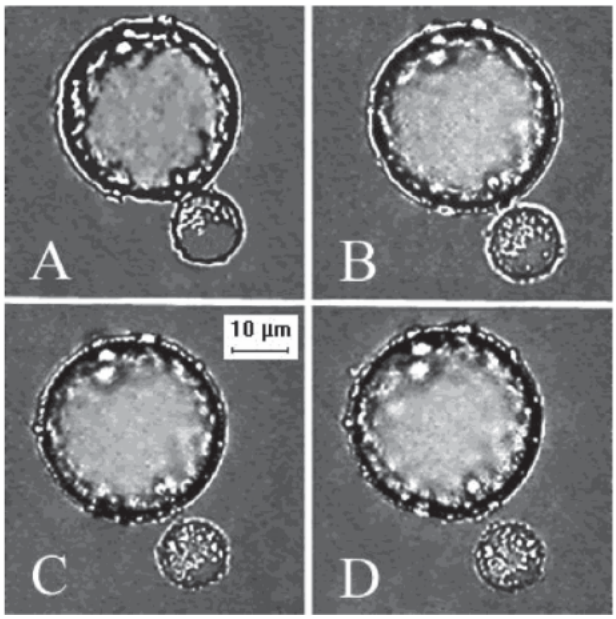

Figure 2. The redistribution of silica particles at the octanol droplet surface over time (in order from A to D). Brighter regions on the smaller droplet indicate trapped-particle locations. Reproduced with permission.[46] Copyright 2003, American Chemical Society.

3. Preparation of Pickering Emulsions

As shown in Equation (1), the high energy required to remove adsorbed particles from the interface results in the superior stability of Pickering emulsions compared with surfactant-stabilized emulsions.[51] On the other hand, in most cases, in order to prepare a stable Pickering emulsion, the high energy barrier also needs to be overcome or decreased by applying external forces or choosing the appropriate conditions. For example, utilizing the electrostatic attraction between the particles and the oil-water interface to make the energy barrier for adsorption very low (relative to kT) or zero.

Recent research has focused on the formation process and adsorption dynamics of particles at the interface, through the development of microscopic and microfabrication technology. For example, under some circumstances, the particles in Pickering emulsions would form bridging between two droplets. French et al. used freeze-fracture scanning electron microscopy (FFSEM) to directly observe the formation of particle bridging between droplets.[52] They found that the formation and destruction of particle bridging were affected by the particle wettability and shear force. Moreover, particle bridging might play an important role in the formation of Pickering emulsion, at least in some formation processes. Using particle bridging in Pickering emulsions, high internal phase emulsions (HIPEs) were developed.[53] Using digital holographic microscopy, Kaz et al. recorded the trajectories of polystyrene particles from the aqueous phase to the w/o interface and measured the adsorption dynamics.[54] When no external energy (or weak energy) was supplied, the binding dynamics of the particles was very slow and the equilibration of particles at the interface between the two phases was a time-consuming process. Thus, in order to prepare Pickering emulsions, a preparation method having enough external energy to overcome the energy barrier is necessary, such as homogenization or sonication.[55–57]

The high mechanical shear used in homogenization and sonication helps overcome the energy barrier, but also breaks the aggregates of nanoparticles and results in a high polydispersity of the emulsion droplets. Moreover, the high polydispersity of droplets can also lead to coalescence and decreased stability of the resulting emulsions, which restricts intensively theoretical research and prevents the use of these techniques for some applications of Pickering emulsions where narrow droplet size distributions are necessary.

In order to systemically study the stability conditions and rheological properties of Pickering emulsions, Binks et al. investigated the preparation of mono-disperse Pickering emulsions.[19] They adopted a method and the related apparatus known as a Couette mixer, proposed by Bibette, for the preparation of Pickering emulsions.[58]A Couette mixer consists of two concentric cylinders with a syringe pump. First, an emulsion stabilized by surfactants with a narrow size distribution is prepared using the Couette mixer, and then particles are added to replace the adsorbed surfactants on the surface of the droplets; the surfactants are removed from the system by dialysis. However, the preparation procedures required for this method can be cumbersome and time-consuming, and relatively high shear rates have to be adopted.

In order to obtain uniform-sized Pickering emulsions, researchers have also tried to improve the process of homogenization. Yamanaka et al. adopted homogenization to prepare Pickering emulsions stabilized by mercaptocarboxylated gold nanoparticles, and the coefficient of variation (CV) of the droplets was lower than 10% at the optimal rotation speed.[59] However, the emulsion droplets prepared by this method were too large (around 0.5–1.2 mm) and were unsuitable for biomedical applications. By carefully optimizing the operating conditions, such as the operational mode, volume throughput, pressure of the flow streams, and homogenization time, Pickering emulsions with relatively small droplet sizes (tens of micrometers) can be prepared by utilizing high-pressure homogenization.[56] However, the need for strict control of the preparation conditions and the high shear used in this technique still restrict its application, especially in the biomedical field. There is urgent need to develop new techniques for preparing monodisperse Pickering emulsions with a broad scope of application.

In recent years, some new approaches have been gradually developed, such as those using microfluidics and membrane emulsification technology, which can simplify the preparation steps and allow more precise control of droplet size. These technologies differ from bulk emulsification techniques, such as homogenization or stirring. The droplets are formed drop-by-drop using a porous membrane or microfluidic device and are dispersed individually into the continuous phase.

3.1. Preparation of Pickering Emulsions Using Microfluidic Devices

Xu et al. developed a microchannel (MC) emulsification method wherein microfluidic equipment was used to prepare Pickering emulsions.[60] The experimental setup of MC emulsification is shown in **Figure 3**.

The central piece of this equipment is a cross-flow-type silicon MC plate on which there are two micromachined arrays of microchannels that are 7 μm in depth and 13 μm in width. The dispersed phase is pumped into the microchannels and expelled from their exit, which forms spherical droplets due to the dragging force of continuous phase flow. Because the microchannels are fabricated by micromachining and have uniform channel width, the size distribution of the obtained droplets is narrow. In addition, the droplet size can be regulated by changing the flow rate of the mobile phase. Besides the effect on the size distribution of the droplets, the authors found that the preparation method also had an impact on the stability of the emulsions. As stated in Section 2.1, in most research, it was found that particles with strong hydrophilicity/hydrophobicity could not effectively stabilize emulsions. Xu et al. found that using the MC emulsification method, emulsions stabilized by hydrophilic SiO_2 particles were stable for at least several months at room temperature. This might be related to the low shear used in MC emulsification, which would not break the aggregation of SiO_2 particles. Moreover, the aggregates of SiO_2 particles would form a thick layer around the droplets and stabilize the emulsion. On the other hand, the high shear of homogenization would break the particle aggregates and the layer around the droplets is thin, as shown in **Figure 4**.

Using microfluidic devices allows the production of uniform emulsions (typically with CV below 5%), and many researchers have adopted this technique for preparing Pickering emulsions when studying the stabilization mechanism or when preparing materials with special structures.[61–65] Whitby et al. used a microfluidic chip, microscope, and high speed camera to study the difference between emulsions stabilized with surfactants and particles.[63] When the continuous phase flowed slowly, the surfactant- and particle-stabilized emulsions did not behave differently, and the droplets were

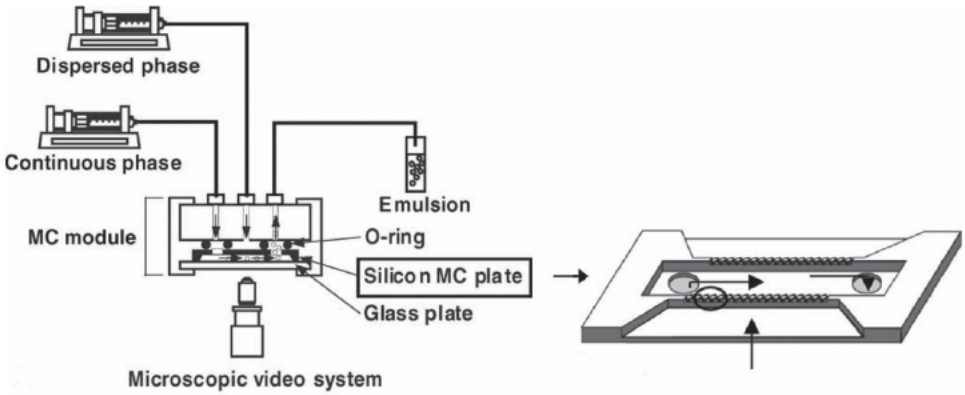

Figure 3. Experimental setup of microchannel (MC) emulsification. Reproduced with permission.[60] Copyright 2005, Elsevier.

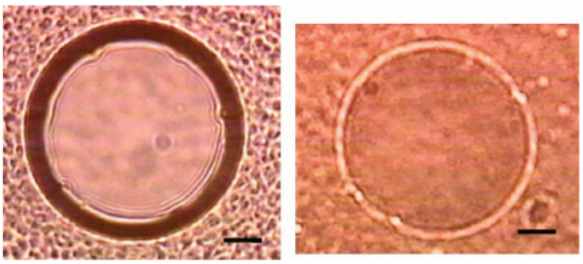

Figure 4. Light microscopy images of the cross-section of droplets prepared by (left) MC emulsification technique and (right) homogenization. Scale bar = 10 m. Reproduced with permission.[60] Copyright 2005, Elsevier.

formed in a dripping mode. However, when the flow rate of the continuous phase increased, the droplets started to neck and rupture, and the two emulsions presented different results. For surfactant-stabilized emulsions, surfactant molecules would accumulate at the neck and would slow the necking dynamics. The rate of neck thinning decreased as the concentration of surfactant increased. In contrast, due to the long time required for particles to diffuse to the newly formed interface, the particles did not play a central role in the early stages of emulsion formation, and the concentration of particles had no significant influence on the size of droplets. Thus, the factors controlling drop size in microfluidic emulsification are very different in surfactant solutions and particle dispersions.

Unfortunately, due to the limitations of the microfluidic equipment, this technique has a low preparation flux and its use in high-throughput production is difficult. Moreover, the flow rate of the continuous phase must be strictly controlled, which would affect the uniformity of droplets when adjusting the rate of adsorption of particles onto droplet surfaces and the rate of detachment of newly formed droplets at the channel exit.

3.2. Preparing Pickering Emulsions by Membrane Emulsification

As shown in **Figure 5**, membrane emulsification (ME) techniques can be divided into four main types: I. direct membrane emulsification (DME); II. premix membrane emulsification (PME); III. Stirred-cell membrane emulsification (SCME); IV. rotational membrane emulsification (RME).

The first two techniques are used more widely than the last two. The main preparation principle for all the ME techniques is pressing the dispersed phase or the pre-emulsified mixture of the dispersed and continuous phase through a microporous membrane. For DME, the dispersed phase is pressed or injected through the membrane into the continuous phase under critical trans-membrane pressure. The preparation process is time-consuming and this technique is suitable for systems with low viscosities. For PME, the dispersed phase and continuous phase are mixed together before use, and the mixed system is pressed through the membrane under high trans-membrane pressure to break up the droplets effectively. The SCME preparation process is somewhat similar to DME, and some research considers SCME and DME to be the same.[69] For RME, the key feature is that the membrane is not stationary; rather, it rotates to induce the detachment of droplets from the membrane. Porous glass membranes have frequently been used as the main components in the first two techniques, with laser-drilled steel membranes being used in the last two techniques. Other types of membranes have also been reported, including ceramic membranes,[70] nickel membranes,[71] and woven metal microscreens.[72] All these membrane emulsification techniques have been used to prepare Pickering emulsions.

Biggs et al. were the first to use ME techniques to prepare Pickering emulsions.[70] They used two types of colloidal silica, viz. 80 nm and 800 nm, as emulsion stabilizers for DME

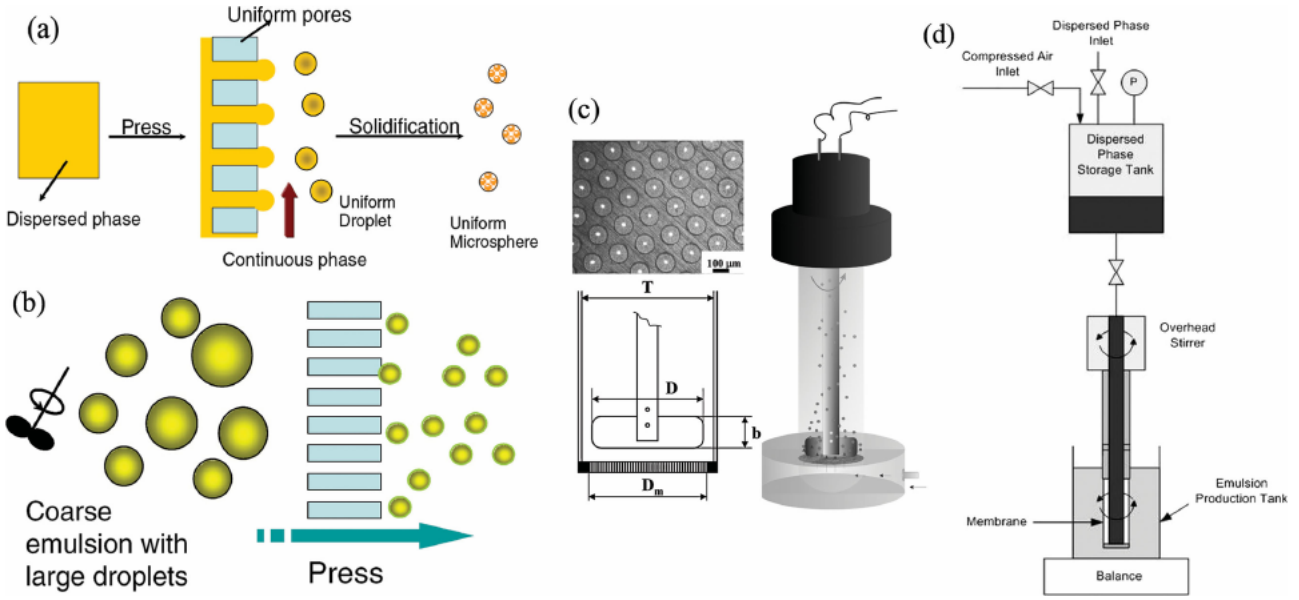

Figure 5. Schematic illustrations of DME (a), PME (b), SCME (c) and RME (d). a,b) Reproduced with permission.[66] Copyright 2014, Elsevier. c) Reproduced with permission.[67] Copyright 2012, Elsevier. Reproduced with permission.[68] Copyright 2014, Elsevier.

and RME, respectively to prepare Pickering emulsions. One important disadvantage of DME is that the continuous phase repeatedly circles the membrane surface. During the cycling process, the droplets break or coalesce, resulting in a broad size distribution of the droplets. In this study, it was found that compared with surfactant-stabilized emulsions, Pickering emulsions have better stability and narrower size distributions even after 30 min of repeated circulation.

Compared with DME, the continuous phase in RME does not re-circulate, avoiding the negative effect on some delicate materials in emulsions. However, the size distributions of emulsion droplets prepared by RME were broader than those of droplets prepared by DME. In order to optimize the RME conditions, Biggs et al. carried out further research.[73] They investigated the effect of pH, electrolyte concentration, membrane rotational speed, and particle concentration. The results showed that the adsorption time of particles onto the interface was the key factor, and that it should be shorter than the critical droplet detachment time to obtain stable, monodisperse emulsions.

In recent years, Ngai and Ma prepared uniform-sized Pickering emulsions by DME and PME.[74,75] First, they used DME techniques to prepare uniform emulsions stabilized by poly(N-isopropylacrylamide-co-methacrylic acid) (PNIPAM-co-MAA) microgels or Kollicoat particles.[74] For both types of particles, uniform-sized and stable Pickering emulsions with CV values lower than 10% were successfully prepared. More importantly, a series of Pickering emulsions with different average sizes and narrow size distributions could be easily prepared by choosing porous membranes with different pore sizes, as shown in **Figure 6**, proving the wide applicability of DME.

However, the droplets produced by DME grow slowly at the end of the membrane pores until they reach a critical value, after which they detach from the surface of the membrane. Thus, a long time is required for emulsion preparation, which is not convenient for large-scale production. The same group investigated the possibility of using high-throughput PME to prepare Pickering emulsions and related microcapsules.[75] They used PME techniques to prepare both the particles and emulsions. The main factors included the trans-membrane pressure, the trans-membrane number, the concentration of particles in the water phase, and the volume ratio of the oil phase to the water phase. Under optimized conditions, microcapsules using Pickering emulsions as templates were prepared with CV values of 23% and average diameters of 9 μm. Since the trans-membrane PME process

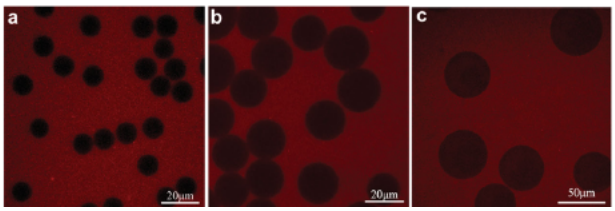

Figure 6. Confocal microscopy images of Pickering emulsions (o/w) prepared by DME using different membrane pore sizes. The pore sizes of the membrane were: a) 2.5, b) 5.2, and c) 9.2 m. The pH of the aqueous phase was 5.7, and PNIPAM-co-MAA microgels were labeled with rhodamine B molecules. Reproduced with permission.[74] Copyright 2014, American Chemical Society.

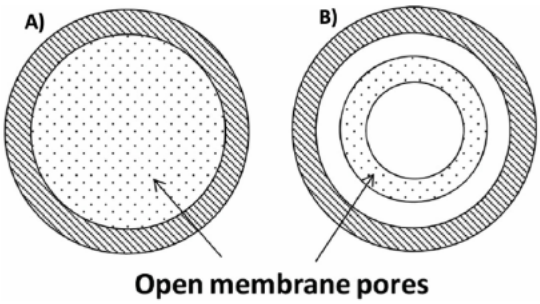

Figure 7. A) Standard membrane, B) annular radial ring membrane. Reproduced with permission.[71] Copyright 2011, American Chemical Society.

can be completed within half an hour and the yield can reach as high as 90% with few damaged microcapsules, PME has great potential for industrial applications.

SCME also has been used to prepare Pickering emulsions by Thompson et al..[71] They used poly(glycerol monomethacrylate)-stabilized polystyrene particles (PGMA-PS) as an emulsion stabilizer that was dispersed in the aqueous phase. The oil phase (sunflower oil) was forced through a nickel film (membrane pore size 5 μm, pore spacing 200 μm) into the aqueous phase to form homogeneous emulsions. By optimizing the stirring rate, particle size, velocity through the membrane, and other factors, uniform Pickering emulsions and related microcapsules were prepared. They found that the size distribution of the emulsions was greatly influenced by the shape of the membrane, and investigated the influence of the shape by using a standard membrane and an annular ring membrane, as shown in **Figure 7**. When the latter was used, a more uniform emulsion was obtained, with a decrease in CV value from 74% to 25%. However, the reduction of the effective area of the annular ring membrane has a negative effect on preparation efficiency.

Comparing membrane and microfluidic emulsification techniques, membrane emulsification can produce droplets at higher throughputs, while the latter technique is advantageous in terms of the uniformity of the prepared emulsions. It is worth noting that both porous membranes and microfluidic devices possess microchannels, and the particles in Pickering emulsions tend to block these channels. Thus, before utilizing these techniques it is necessary to choose the proper particles (e.g., small size) or design the preparation procedures carefully (e.g., adding particles in the continuous phase).

4. The Effect of Particles on the Properties of Pickering Emulsions

The studies on Pickering emulsions have broadened their range of applications and led to the discovery of distinctive properties not found in classical emulsions stabilized by surfactants.

4.1. Stability

One significant advantage of Pickering emulsions is their high stability. As can be seen in Equation (1), when using

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particles with diameters of 0.01–10 μm and intermediate θ as emulsifiers, the particles attach strongly to the interface with high detachment energies (around 10^2–10^6 k_BT). Due to the high energy required to remove the adsorbed particles from the interface, it is well known that Pickering emulsions have superior stabilities compared to surfactant-stabilized emulsions.

Experiments have also proved this point. Velev et al. carried out studies on the preparation of super-stable Pickering emulsions and their rheological properties.[76,77] They used microrod particles as stabilizers and achieved long-term stabilization of emulsions of low-molecular-weight hydrocarbons in water or water in oil systems, which is hard to achieve with regular surfactants. Binks et al. used a mixture of two types of particles with opposite charges to stabilize Pickering emulsions.[78] The particles formed a close-packed monolayer around the droplets and great long-term emulsion stability was achieved. Other research found that emulsions stabilized by starch granules were stable even after two years of storage, with unchanged droplet sizes.[79] The stability of Pickering emulsions is also affected by the preparation process, which affects the droplet size and arrangement of particles at the interface.[80] Emulsions prepared by ultrasonication possess better storage stability than those prepared by vortex mixing. Fluorescent confocal microscopy observations revealed that the particles formed a layer around the droplets and some particles were simultaneously adsorbed onto two adjacent droplets forming a bridge between the two, which prevented coalescence in emulsions prepared by ultrasonication. On the other hand, homogeneous, isolated, and densely packed droplets were observed in emulsions prepared by vortex mixing. Other studies have also investigated the stability of Pickering emulsions against external factors, such as pH, shear, temperature, and salt concentration.[81–85]

In recent years, the applications of Pickering emulsions have broadened to include biomedical fields, and rapid development has been seen in this area. Most commercial products in biomedical fields need to be stored at low temperatures or freeze-dried to maintain the bioactivity of biomolecules, and destabilization of emulsions frequently occurs due to crystallization of the water and oil phases.[8] In one study carried out by Marefati et al., the stability of Pickering emulsions stabilized with starch granules during freezing and freeze-drying processes was investigated.[86] Pickering emulsions that were slowly frozen at −18 °C showed excellent freeze-thaw stabilities, and the size distribution of rehydrated droplets did not change. The freeze-thaw stability of other Pickering emulsions has also been reported.[87,88] However, the relevant research is still incomplete and more systematic studies need to be carried out in the future. Moreover, for biomedical applications, the systems need to be biocompatible and preferably biodegradable. If the particles could be degraded in aqueous solution, the change in their properties would affect their capacity for stabilizing emulsions and may even result in destabilization. However, at present, most studies are still in the laboratory stage and this issue has not been widely brought to the attention of researchers.

4.2. Permeability

The surfaces of droplets in Pickering emulsions are covered by particles, and due to the relatively large sizes of the particles (usually tens of nanometers to several micrometers) in comparison to surfactant molecules (0.4–1 nm),[89] there are relatively large spaces between them.[90] The pore radius R_p depends on the particle radius b and the colloidal volume fraction in the shell ϕ, approximated by $R_p = b\{(\pi/6\phi)^{1/3}-1\}$.[91]

The high permeability of Pickering emulsions is a double-edged sword. On one hand, it facilitates molecule and energy exchange between the interior and the external surroundings; on the other hand, this semi-open structure of Pickering emulsions or of materials prepared using Pickering emulsions as templates is unfavorable for the entrapment and protection of bioactive molecules, especially those with low molecular weights. For example, the high permeability of colloidosomes was found to result in the loss of their cargo before their target was reached.[92] Moreover, the porous structure of materials prepared using Pickering emulsions as templates also decreases their mechanical strength.[93]

Several methods can be utilized to adjust the permeability of Pickering emulsions, including using particles with different sizes, increasing the particle concentration to increase the thickness of the particle shell, and using deformable particles or particle aggregates.[90,94,95]

Sjöö et al. used starch granules, which could swell during gelatinization, to prepare Pickering emulsions, and this property could be useful to tune and control the permeability of capsules.[90] Heating the starch granules caused them to swell and gelate, and when the granules were partially gelatinized, they formed a more impermeable layer around the emulsion droplets compared with unheated emulsions. Nan et al. combined the PME and polymer deposition methods to prepare Pickering emulsions and the related colloidosomes with high yields and low permeabilities.[75] The principle of the polymer deposition method is illustrated in **Figure 8**.[96] The

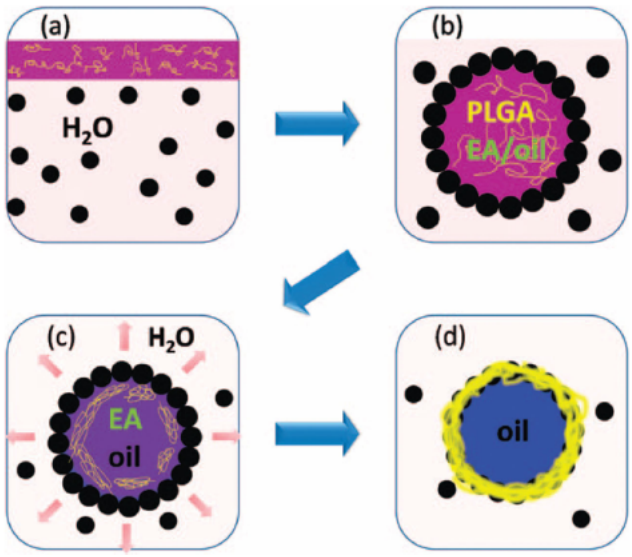

Figure 8. Schematic showing the principle of the polymer deposition method for preparation of capsules. Reproduced with permission.[96] Copyright 2009, American Chemical Society.

Pickering emulsions were prepared first, and then a polymer was precipitated at the interface to lock the assembled particles into a polymeric shell. Using the polymer deposition method, the interstitial voids were decreased and the insulin encapsulation efficiency of colloidosomes was increased by up to 96.7% compared with PLGA particles prepared using surfactant-stabilized emulsions as templates.[75]

Moreover, the adjustable permeability of Pickering emulsions and related materials provides distinctive advantages for some applications. For example, using stimuli-responsive particles to prepare Pickering emulsions, the permeability of the microcapsules can be adjusted under different circumstances. Behrens et al. used pH-responsive particles to prepare w/o, o/w, and w/o/w Pickering emulsions and colloidosomes.[92,97] The permeability of the colloidosomes changed greatly with pH and the colloidosomes even deformed or dissolved under some circumstances.[98] This property would be useful when colloidosomes are used as a site-specific delivery system, such as in tumor or colon target delivery systems.

4.3. Toxicity

Many low-molecular-weight surfactants give rise to several biological side effects, of which acute hypersensitivity reactions, peripheral neurotoxicity, and membrane-damaging effects are the most frequently reported.[99–103] It is well known that using particles to replace surfactants will decrease the irritation and toxicity related to surfactants.[104,105] For example, silica-based colloidosomes with a polymer core were prepared using Pickering emulsions as templates and used as implantable drug carriers.[106] Retinoic acid was used as a model drug and entrapped in the colloidosomes. The effect of drugs on zebrafish development and tail regeneration was investigated. The drug-loaded colloidosomes showed excellent biocompatibility without inflammation at the injection site. Ziener et al. reported the effects of the surface roughness of nanoparticles prepared using particles or surfactants as stabilizers on cell uptake.[107] They found that the surface roughness of particles increased when using Pickering emulsions as templates. The increased roughness of the particles resulted in decreased uptake in Hela cells and affected the endocytotic uptake routes, which would possibly affect the toxicity of the particles.

However, there have been very few reports regarding the cell toxicity, distribution, and in vivo metabolism of Pickering emulsions because the majority of research has focused on formulation design and in vitro evaluation. In recent years, concerns about the biological toxicity of nanomaterials have been a good reminder to study the toxicity of Pickering emulsions.[108] Most Pickering emulsions are stabilized by nanoscale particles and the nanotoxicity of those particles is not negligible. Nanoparticles administered by intravenous injection could be distributed to the lung, bone marrow, liver, spleen, and the lymphatic system.[109] After systemic circulation, nanoparticles are cleared by the liver and splenic macrophages. The accumulation of particles in the liver and spleen may result in a degradation burden and damage to these organs.

5. Biomedical Applications of Pickering Emulsions

Despite the difficulties of Pickering emulsions described above, they still have potential as functional emulsion candidates for various applications. Pickering emulsions have been reported in cosmetics, foods, flooding agents, and biocatalysts.[110–116] In recent years, their use in biomedical fields has attracted significant research interest, including the direct use of Pickering emulsions and of materials fabricated using Pickering emulsions as templates. In the following sections, some examples of the application of these two aspects of Pickering emulsions in biomedicine are given.

5.1. Direct Biomedical Applications of Pickering Emulsions

Biomedical applications of Pickering emulsions have been reported in hundreds of studies, which includes studies on injection, topical or oral administration, and so on. Yang et al. developed paclitaxel-loaded nanoscale emulsion droplets stabilized by deformable poly(N-isopropylacrylamide-co-allylamine) (PNIAM-co-AA) nanogels.[117] The nanodroplets were administrated to Wistar rats via intravenous injection, and the tissue distribution and antitumor efficacy studies proved that this Pickering emulsion formulation was promising as a drug delivery system for cancer therapy. However, at present, there are not many relevant studies on the use of Pickering emulsions via the injection route. Most of the direct biomedical applications of Pickering emulsions fall into two main categories: topical and oral drug delivery systems.

5.1.1. Topical Drug Delivery Systems

The use of Pickering emulsions as topical drug delivery systems has been studied, and some related reviews have been published.[118,119] Chevalier et al. used silica particles as a stabilizing agent to prepare w/o Pickering emulsions and deliver hydrophilic drugs by transdermal administration using pig skin as an in vitro skin model.[120] They found that Pickering emulsions could deliver drugs more efficiently, with threefold higher permeation rates than classical emulsions stabilized by surfactants. The main reason might be the stronger adhesive forces between Pickering emulsions and skin, and the penetration of particles into the skin, which enhanced the effectiveness of drug delivery. They further investigated the potential of o/w emulsions stabilized with particles or surfactants as topical delivery systems for lipophilic drugs.[121] In this experiment, although the total amount of drug absorbed in the skin after 24 h was not significantly different for classical and Pickering emulsions, the latter could promote high storage in the stratum corneum and slowly release the drug to deeper skin layers.

Besides silica particles, starch granules and cyclodextrins have also been used as emulsion stabilizers for topical formulations.[122–124] Wahlgren et al. used biocompatible starch granules to prepare Pickering emulsions with three different oils (Miglyol, paraffin, and shea nut oil) for topical

applications.[123] They found that the type of oil did not affect transdermal diffusion in in vitro tests, and that using emulsions could increase the flux of skin diffusion compared to solution formulations.

5.1.2. Oral Drug Delivery Systems

Research into the use of Pickering emulsions in food started about a decade ago, and according to several reviews, using particles instead of surfactants has advantages in terms of physical stability against storage, temperature, oxidation, and digestion.[125–127] Inspired by this research, the potential of Pickering emulsions as oral drug delivery systems was investigated. Chitosan nanoparticles crosslinked with tripolyphosphate were prepared and utilized to create encapsulated curcumin emulsions.[128] Encapsulation with Pickering emulsions increased the stability of curcumin against degradation and allowed pH-responsive release. Nitin et al. also encapsulated curcumin in Pickering emulsions stabilized by silica particles.[129] In this study, the stability of curcumin during storage in the emulsion system was 100 times higher than that of curcumin in distilled water. It is worth noting that an MTT assay showed that 88.2 ± 1.73% of the cells retained their viability upon exposure to Pickering emulsion for 24 h. Further examination proved that the Pickering emulsion droplets were taken up effectively by epithelial cells, as shown in **Figure 9**. This phenomenon requires deeper analysis, but could prove to be very useful for oral or nasal drug delivery due to the enhanced drug absorption.

Other researchers also published studies on Pickering emulsions as oral drug delivery systems.[130,131] Lesmes et al. prepared silica nanoparticle-stabilized Pickering emulsions, and this system showed exceptional stability at pH values of 3 to 7, providing better protection than lipid droplets.[130] These characteristics of Pickering emulsions make them potential oral drug delivery agents.

Besides their use as topical and oral drug delivery systems, Pickering emulsions have also been applied for photoacoustic imaging and photothermal therapy. Photoacoustic imaging is a technique that uses the optical spectra of absorbers in the body, such as microbubbles or hemoglobin, to provide image contrast under external excitation using laser or ultrasound. However, it is hard to acquire single-shot images due to the low efficiency of photoacoustic signal generation. The utilization of Pickering emulsions in photoacoustic imaging provides a possible solution. In Pickering emulsion systems, the particles cluster in emulsion droplets, which results in a high signal when they are excited, even at low agent concentrations. The O'Donnell group published several papers about the development of Pickering nanoemulsions stabilized by gold nanoparticles and their application as contrast-enhanced imaging agents.[132–134] Under optimized conditions, ultrasensitive and specific imaging of nanoagents was carried out even at low concentrations (below 7 pM). However, most studies into this are currently in the in vitro evaluation stage, and further in vivo study, especially on tissue distribution and the metabolism of particles after absorption, will be necessary to evaluate the feasibility of using Pickering emulsions in biomedicine.

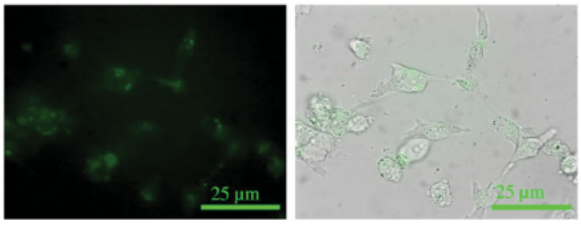

Figure 9. Wide-field fluorescence (left) and fluorescence-DIC overlay (right) images of an epithelial cancer cell line (MDA-MB-231 cells) after 24 h incubation with nile-red encapsulated Pickering emulsion (400 ×). Reproduced with permission.[129] Copyright 2013, Elsevier.

5.2. Pickering Emulsions as Templates to Prepare Materials used in Biomedicine

Due to the inconvenience of directly using emulsion formulations in biomedicine, the biomedical application of materials using Pickering emulsions as templates has been reported more frequently. The advantages are mainly the low toxicity due to the surfactant-free preparation process and the flexibility of using various particles as stabilizers. For example, Maas et al. prepared colloidosomes by using particles to replace the surfactant.[135] The preparation process was mild and avoided any other toxic additives. The pore shape and thickness of the colloidosome layer was adjustable, providing a versatile carrier for proteins, antibodies, and other drugs. In recent years, biomedical applications of materials based on Pickering emulsions, especially colloidosomes, have developed greatly, and can be divided into three main categories as follows:

5.2.1. Stimuli-Sensitive Materials as Drug Delivery Systems

In drug delivery systems, protection of the drug with slow or no leakage during storage, and its rapid and controlled release when being used are necessary. In order to achieve this, the use of stimuli-sensitive nanoparticles to prepare Pickering emulsions and colloidosomes has attracted considerable attention. Various external factors can be used to trigger the burst release of drugs, including pH, temperature, salt, light, and bioactive molecules.[136–140] Among these, pH is one of the most widely investigated external stimuli. Using pH-sensitive nanoparticles in the shell of colloidosomes, the shape, volume, or permeability of the colloidosomes can be changed by adjusting the external pH.[141,142] These pH-sensitive colloidosomes could be used as oral drug delivery systems. For example, Nan et al. prepared a chitosan-coated alginate particle-stabilized Pickering emulsion and used it as a template to create insulin-loaded colloidosomes.[75] Due to the pH-sensitivity of the chitosan-coated alginate particles, the prepared colloidosomes also possessed pH-sensitivity and released insulin slowly in simulated gastric fluid (SGF, pH 1.2) and quickly in simulated intestinal fluid (SIF, pH 6.8). In vivo tests proved that the colloidosomes had an effective hypoglycemic effect, as shown in **Figure 10**.

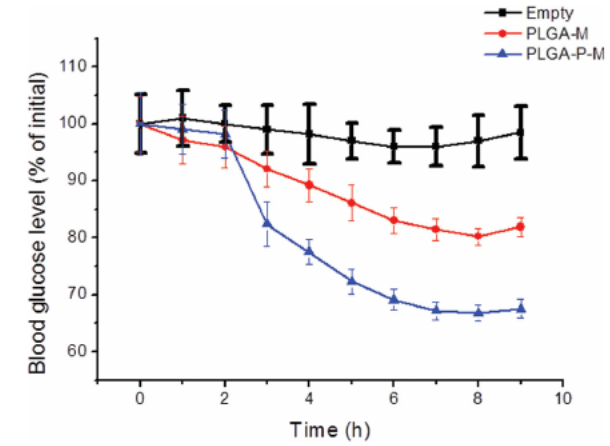

Figure 10. Profiles of blood glucose levels of rats vs time after oral administration of empty colloidosomes (Empty), PLGA particles prepared using classical emulsions as a template (PLGA-M) and colloidosomes prepared using Pickering emulsions as a template (PLGA-P-M) (n = 6). Reproduced with permission. [75] Copyright 2014, Royal Society of Chemistry.

Besides pH, temperature is another important external stimulus that has been utilized to trigger drug release from colloidosomes. Poly(N-isopropylacrylamide) (PNIPAm) nanoparticles are the most frequently used particle emulsifiers for the preparation of thermally responsive colloidosomes. PNIPAm particles display obvious thermal sensitivity, rapidly shrinking when the temperature is raised above their lower critical solution temperature (LCST). When colloidosomes are prepared using PNIPAm nanoparticles, they exhibit thermo-sensitive behavior similar to that of PNIPAm nanoparticles, as shown in **Figure 11**. [64]

In some research, PNIPAm was not used in the formulation of nanoparticles, and was instead used as a polymer with other nanoparticles to form the capsule shell.[143,144] The drug inside the capsules was released slowly at low temperatures (e.g., 25 °C), and when the temperature was raised above the LCST of PNIPAm, the release rate increased due to shrinkage of the capsules, which squeezed the drug out of the shell through the pores between the particles. [143]

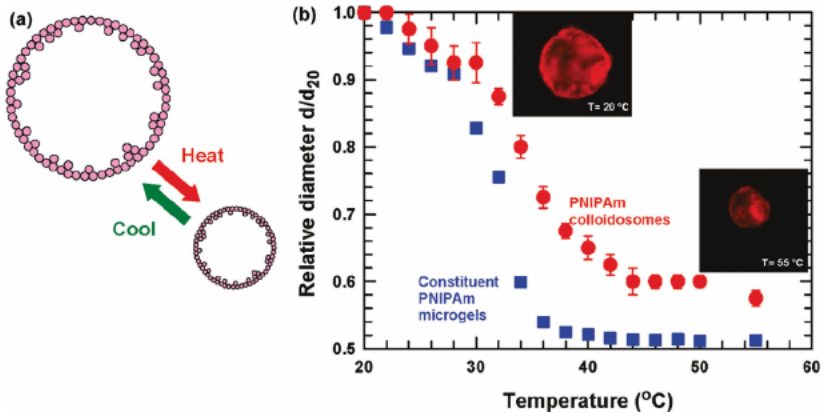

Figure 11. a) Schematic representation of the thermoresponsive behavior of a colloidosome-PNIPAm nanoparticle shell. b) Equilibrium size change of PNIPAm colloidosomes and their constituent PNIPAm microgels. Size data of three different colloidosomes were averaged for better statistics. Reproduced with permission. [64] Copyright 2010, American Chemical Society.

For these stimuli-sensitive colloidosomes/capsules, the driving force behind drug release was the deformation of the shell or colloidosome.[145] In some circumstances, deformation might be unfavorable and needs to be avoided. Zhou et al. developed a novel method to obtain stimuli-sensitive colloidosomes without shell deformation.[146] The thermo-sensitive triblock copolymer polyethylene glycol-poly(*p*-phenylene oxide)-polyethylene glycol (PEO–PPO–PEO) was dissolved in the aqueous cores of the colloidosome and adsorbed on the surfaces of the nanoparticles of the colloidosome shell to block the pores between the nanoparticles. At sufficiently high temperatures, the polymer was desorbed from the nanoparticles and the pores opened, releasing the encapsulated drug. Moreover, since the desorbed tri-polymer remained inside the colloidosomes, the process of opening/closing the pores was reversible, which facilitates their application. However, for those studies, toxic and non-biodegradable polymers like PNIPAm have frequently been used, which restricts their practical clinical application.

5.2.2. Materials with High Surface Areas for Biosensing or Bioimaging

With the development of material science, some new particles have also proved useful for preparing Pickering emulsions and related materials, such as quantum dots and graphene oxide.[147–150] Kim et al. reported the use of highly luminescent graphene quantum dots as stabilizers to produce Pickering emulsions and particles with controlled nanostructures and high luminescence, which would be useful for bioimaging, drug delivery, and optoelectronic devices.[151]

Moreover, since colloidosome shells are usually composed of hundreds or thousands of nanoparticles, a predominant advantage of colloidosomes over other capsules with smooth surfaces is the large surface area, which facilitates the grafting of functional groups or makes possible other applications needing large surface areas, such as biosensing or bioimaging. Ling et al. used plasmonic Ag nanocubes to prepare colloidosomes as surface enhanced Raman scattering (SERS) platforms for sub-microliter toxin sensing.[152] The colloidosomes, whose surface area enhancement was more than 26 times that of the original water droplet, showed impressive ultratrace detection abilities for both aqueous- and organic-soluble toxins, even down to sub-femtomole levels. The colloidosomes also showed super-stability against storage and external shear forces.

With the development of preparation methods and nanoparticles, colloidosomes with special structures have been continuously developed, which further broadens the range of fields in which they can be applied and improves their performance. Maas et al. reported colloidosomes with two types of nanoparticles (superparamagnetic iron oxide and fluorescent silica

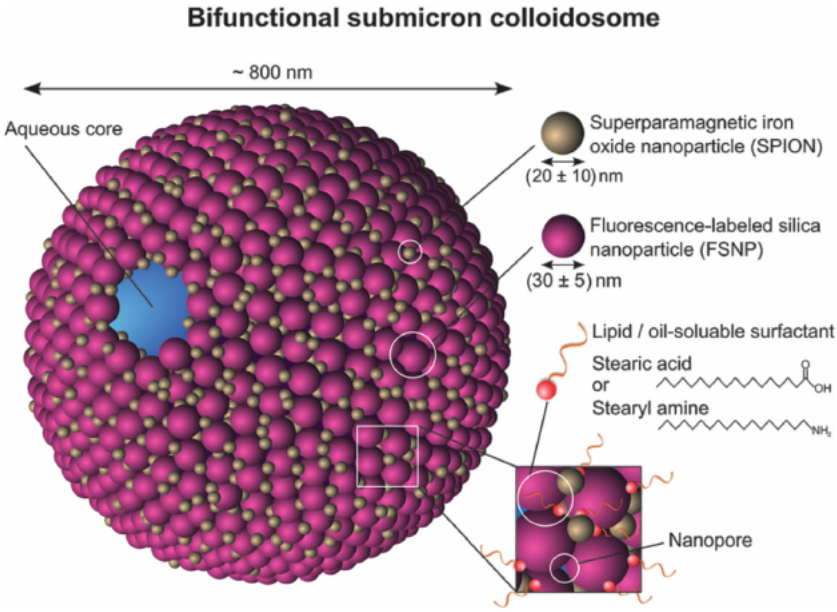

Figure 12. Schematic illustration of colloidosomes with fluorescence-labeled silica nanoparticles and superparamagnetic iron oxide nanoparticles on the shell. Reproduced with permission.[153] Copyright 2015, Wiley-VCH Verlag GmbH & Co. KGaA.

nanoparticles) on their shells, as shown in **Figure 12**.[153] The bifunctionality produced by incorporating both fluorescence and superparamagnetism in a single sub-micrometer colloidosome would be useful for various biomedical applications, including biosensing, bioimaging, magnetic fluid hyperthermia (MFH), and magnetic particle imaging (MPI).

Ye et al. developed a Cu(I)-catalyzed click reaction to prepare colloidosomes from molecularly imprinted polymer nanoparticles and fluorogenic boronic acid. The high molecular selectivity and fluorescence response of the resulting colloidosomes afforded the possibility of their use as a biosensing or bioseparation medium.[154]

Although investigation of the toxicity, action mechanism, and metabolic processes as well as practical application of these materials might take a long time, we believe that with the development of materials science, biology, and supporting techniques, these materials will have clinical applications in the future.

5.2.3. Materials with Proper Permeability for use as Bioreactors

Colloidosomes with particle-composed shells are penetrable, which facilitates the exchange of molecules and energy between the interior and exterior of the colloidosomes. This property is especially useful when the materials are used as bioreactors or artificial cells. Dan presented two equations (Equations (4) and (5)) for calculating the permeability of small molecules from colloidosomes for use with monolayers or multi-layers, respectively.[155]

For colloidosomes with a monolayer, where the shell thickness h is equal to $2b$ (b, particle radius), the permeability A is:

$$A = 3D_s/Rb = \{3D^*\pi(1-\phi)\}/(2\alpha_c R^2\phi) \quad (4)$$

Where D_S is the diffusion coefficient through the shell, R is the radius of the colloidosome core, D^* is the diffusion coefficient through the voids (water, polymer binder, etc.), ϕ is the colloidal volume fraction in the shell, and α_c accounts for the pore structure.

For colloidosomes with multilayers, where the shell thickness h is much smaller than the core radius R, the permeability is given by:

$$A = 3D_s/Rh = \{3D^*\pi b(1-\phi)\}/(2\alpha_c R^2 h\phi) \quad (5)$$

Equations (4) and (5) show that the permeability of a colloidosome can be adjusted by varying the particle radius or particle concentration. Colloidosomes with proper permeability could not only maintain the bioactivity of an entrapped enzyme, bacteria, or cell, but also enhance their stability against hostile conditions. Zhu et al. encapsulated laccase in colloidosomes as an enzymatic bioreactor to enhance the stability and reusability of the enzyme in organic reaction media.[156] They found that after six consecutive recycling runs under optimized conditions, 60% of the initial activity still remained for laccase-loaded colloidosomes. Routh at the University of Cambridge performed further work on this subject. The group headed by him encapsulated various bacteria, cells, and enzymes, such as amylase, lactic acid bacteria, and yeast cells, in colloidosomes.[157–159]

Besides their use as bioreactors, Li et al. constructed bioinorganic protocells based on colloidosomes.[160,161] They found that the rate of in vitro expression of enhanced green fluorescent protein (eGFP) was the same for the colloidosome interior and bulk aqueous solution. Moreover, the encapsulation of the enzymes in colloidosomes enhanced their bioactivity. Subsequently, the same group developed the electrostatically gated membrane permeability of protocells, which enhanced their performance and broadened their applicability.

6. Conclusion

Pickering emulsions have many advantages over classical emulsions, including high stability, low toxicity, and the variety of particles available, all of which have promoted their study and potential applications, especially in biomedicine. Novel Pickering emulsions and related materials are constantly emerging, such as non-spherical emulsions or those prepared using non-spherical particles.[162–164] Many researchers have performed valuable work in this field. For example, Sander and Studart prepared nanoparticle-filled colloidosomes with tunable cargo release profiles.[165] pH-sensitive nanoparticles can release adsorbed drugs slowly or swell rapidly to burst-release the drugs under proper pH stimulation. The unique structure of colloidosomes provides control of the release mode for different needs.

However, most of these studies are still at the stage of lab research and small-scale experiments. In order to use those

particles in clinical trials, several obstacles need to be conquered. Firstly, most biodegradable particles are ideally not hard, smooth, or spherical particles and differ from the classical silica and latex particles that are usually used for stabilizing Pickering emulsions. In addition, the introduction of these particles increases the difficulty and complexity of preparing Pickering emulsions. Secondly, further systematic research needs to be carried out on the mechanism of action and metabolic behavior of Pickering emulsions as drug carriers. Although there are many studies on biomedical formulations based on particles or emulsions, there has been little research into the synergistic effects of particles and emulsions as a whole formulation. Moreover, few studies are at the stage of in vitro evaluation. Thirdly, size control of Pickering emulsions is more difficult than for emulsions stabilized using surfactants, especially with high particle contents or large particle sizes. The development of membrane emulsification and microfluidic methods has partly solved this problem, but there are still many challenges to large-scale production. Without narrow size distributions, the utilization and evaluation of Pickering emulsions would be difficult. The development of Pickering emulsions needs the cooperation of material and medical scientists. We believe that with the development of material technology and a comprehensive understanding of the formation and action mechanisms of Pickering emulsions, these emulsions will usher in a new period of rapid development.

Acknowledgements

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[1] W. Ramsden, *Proc. R. Soc. London* **1903**, *72*, 156.
[2] S. U. Pickering, *J. Chem. Soc.* **1907**, *91*, 2001.
[3] R. Aveyard, B. P. Binks, J. H. Clint, *Adv. Colloid Interface Sci.* **2003**, *100–102*, 503.
[4] A. D. Dinsmore, M. F. Hsu, M. G. Nikolaides, M. Marquez, A. R. Bausch, D. A. Weitz, *Science* **2002**, *298*, 1006.
[5] O. D. Velev, K. Furusawa, K. Nagayama, *Langmuir* **1996**, *12*, 2374.
[6] Z. Li, T. Ming, J. Wang, T. Ngai, *Angew. Chem. Int. Edit.* **2009**, *48*, 8490.
[7] S. Lam, K. P. Velikov, O. D. Velev, *Curr. Opin. Colloid In.* **2014**, *19*, 490.
[8] M. Rayner, D. Marku, M. Eriksson, M. Sjöö, P. Dejmek, M. Wahlgren, *Colloid. Surface. A* **2014**, *458*, 48.
[9] S. H. Piao, S. H. Kwon, W. L. Zhang, H. J. Choi, *Soft Matter* **2015**, *11*, 646.
[10] J. Tang, P. J. Quinlan, K. C. Tam, *Soft Matter* **2015**, *11*, 3512.
[11] C. C. Berton-Carabin, K. Schroën, *Ann. Rev. Food Sci. Technol.* **2015**, *6*, 263.
[12] M. Wahlgren, J. Engblom, M. Sjöö, M. Rayner, *Curr. Pharm. Biotechno.* **2013**, *14*, 1222.
[13] B. P. Binks, T. S. Horozov, *Colloidal Particles at Liquid Interfaces*, Cambridge University Press, Cambridge, UK **2007**.
[14] T. Ngai, S. Bon, *Particle-Stabilized Emulsions and Colloids: Formation and Applications*, Royal Society of Chemistry, London, UK **2014**.
[15] B. P. Binks, *Curr. Opin. Colloid In.* **2002**, *7*, 21.
[16] B. P. Binks, S. O. Lumsdon, *Langmuir* **2000**, *16*, 8622.
[17] V. B. Menon, D. T. Wasan, *Colloids Surf.* **1988**, *29*, 7.
[18] D. E. Tambe, M. M. Sharma, *Adv. Colloid Interface Sci.* **1994**, *52*, 1.
[19] J. Giermanska-Kahn, V. Schmitt, B. P. Binks, F. Leal-Calderon, *Langmuir* **2002**, *18*, 2515.
[20] B. P. Binks, J. H. Clint, *Langmuir* **2002**, *18*, 1270.
[21] F. Tu, B. J. Park, D. Lee, *Langmuir* **2013**, *29*, 12679.
[22] A. W. Dipl.-Chem, M. Hoffmann, A. H. E. Müller, *Angew. Chem. Int. Edit.* **2008**, *47*, 711.
[23] W. Cao, R. Huang, W. Qi, R. Su, Z. He, *ACS Appl. Mater. Interfaces* **2015**, *7*, 465.
[24] D. O. Grigoriev, J. Krägel, V. Dutschk, R. Miller, H. Möhwald, *Phys. Chem. Chem. Phys.* **2007**, *9*, 6447.
[25] E. Nowak, G. Combes, E. H. Stitt, A. W. Pacek, *Powder Technol.* **2013**, *233*, 52.
[26] L. N. Arnaudov, O. J. Cayre, M. A. C. Stuart, S. D. Stoyanov, V. N. Paunov, *Phys. Chem. Chem. Phys.* **2010**, *12*, 328.
[27] J. S. Weston, R. E. Jentoft, B. P. Grady, D. E. Resasco, J. H. Harwell, *Ind. Eng. Chem. Res.* **2015**, *54*, 4274.
[28] B. P. Binks, S. O. Lumsdon, *Langmuir* **2001**, *17*, 4540.
[29] F. Nan, J. Wu, F. Qi, Y. Liu, T. Ngai, G. Ma, *Colloid. Surface. A* **2014**, *456*, 246.
[30] F. Qi, J. Wu, G. Sun, F. Nan, T. Ngai, G. Ma, *J. Mater. Chem. B* **2014**, *2*, 7605.
[31] S. Fujii, M. Okada, T. Furuzono, *J. Colloid Interf. Sci.* **2007**, *315*, 287.
[32] Z. Wei, C. Wang, H. Liu, S. Zou, Z. Tong, *J. Appl. Polym. Sci.* **2012**, *125*, E358.
[33] K. L. Thompson, L. A. Fielding, O. O. Mykhaylyk, J. A. Lane, M. J. Derry, S. P. Armes, *Chem. Sci.* **2015**, *6*, 4207.
[34] Y.-H. Yu, Y.-P. Chen, M. Zeng, Z. Cheng, *Mater. Lett.* **2016**, *163*, 158.
[35] J. W. J. de Folter, E. M. Hutter, S. I. R. Castillo, K. E. Klop, A. P. Philipse, W. K. Kegel, *Langmuir* **2014**, *30*, 955.
[36] T. Yamagami, Y. Kitayama, M. Okubo, *Langmuir* **2014**, *30*, 7823.
[37] B. Madivala, J. Fransaer, J. Vermant, *Langmuir* **2009**, *25*, 2718.
[38] V. R. Dugyala, S. V. Daware, M. G. Basavaraj, *Soft Matter* **2013**, *9*, 6711.
[39] I. Kalashnikova, H. Bizot, B. Cathala, I. Capron, *Langmuir* **2011**, *27*, 7471.
[40] M. Luo, G. K. Olivier, J. Frechette, *Soft Matter* **2012**, *8*, 11923.
[41] M. E. Flatté, A. A. Kornyshev, M. Urbakh, *J. Phys. Chem. C* **2010**, *114*, 1735.
[42] F. Reincke, W. K. Kegel, H. Zhang, M. Nolte, D. Wang, D. Vanmaekelbergh, H. Möhwald, *Phys. Chem. Chem. Phys.* **2006**, *8*, 3828.
[43] K. Larson-Smith, A. Jackson, D. C. Pozzo, *Langmuir* **2012**, *25*, 2493.
[44] J. W. O. Salari, F. A. M. Leermakers, B. Klumperman, *Langmuir* **2011**, *27*, 6574.
[45] J. W. O. Salari, G. Mutsaers, J. Meuldijk, B. Klumperman, *Langmuir* **2014**, *30*, 7327.
[46] E. Vignati, R. Piazza, *Langmuir* **2003**, *19*, 6650.
[47] A. San-Miguel, S. H. Behrens, *Langmuir* **2012**, *28*, 12038.
[48] M. K. Mulligan, J. P. Rothstein, *Langmuir* **2011**, *27*, 9760.
[49] S. Arditty, C. P. Whitby, B. P. Binks, V. Schmitt, F. Leal-Calderon, *Eur. Phys. J. E* **2003**, *11*, 273.
[50] B. R. Midmore, *Colloid. Surface. A* **1998**, *132*, 257.
[51] C. P. Whitby, H. K. Anwar, J. Hughes, *J. Colloid Interf. Sci.* **2016**, *465*, 158.
[52] D. J. French, P. Taylor, J. Fowler, P. S. Clegg, *J. Colloid Interf. Sci.* **2015**, *441*, 30.

[53] A. Gossard, G. Toquer, A. Grandjean, J. Causse, *Colloid. Surface. A* **2014**, *462*, 162.
[54] D. M. Kaz, R. McGorty, M. Mani, M. P. Brenner, V. N. Manoharan, *Nat. Mater.* **2012**, *11*, 138.
[55] A. Kaiser, T. Liu, W. Richtering, A. M. Schmidt, *Langmuir* **2009**, *25*, 7335.
[56] K. Köhler, A. S. Santana, B. Braisch, R. Preis, H. P. Schuchmann, *Chem. Eng. Sci.* **2010**, *65*, 2957.
[57] B. Duncan, R. F. Landis, H. A. Jerri, V. Normand, D. Benczédi, L. Ouali, V. M. Rotello, *Small* **2015**, *11*, 1302.
[58] C. Mabille, V. Schmitt, Ph. Gorria, F. Leal Calderon, V. Faye, B. Deminière, J. Bibette, *Langmuir* **2000**, *16*, 422.
[59] K. Yamanaka, S. Nishino, K. Naoe, M. Imai, *Colloid. Surface. A* **2013**, *436*, 18.
[60] Q. Y. Xu, M. Nakajima, B. P. Binks, *Colloid. Surface. A* **2005**, *262*, 94.
[61] A. B. Subramaniam, M. Abkarian, H. A. Stone, *Nat. Mater.* **2005**, *4*, 553.
[62] N. Hassan, A. Stocco, A. Abou-Hassan, *J. Phys. Chem. C* **2015**, *119*, 10758.
[63] C. Priest, M. D. Reid, C. P. Whitby, *J. Colloid Interf. Sci.* **2011**, *363*, 301.
[64] R. K. Shah, J.-W. Kim, D. A. Weitz, *Langmuir* **2010**, *26*, 1561.
[65] Z. Nie, J. Park, W. Li, S. A. F. Bon, E. Kumacheva, *J. Am. Chem. Soc.* **2008**, *130*, 16508.
[66] G. Ma, *J. Control. Release* **2014**, *193*, 324.
[67] M. M. Dragosavac, R. G. Holdich, G. T. Vladisavljević, M. N. Sovilj, *J. Membrane Sci.* **2012**, *392–393*, 122.
[68] D. M. Lloyd, I. T. Norton, F. Spyropoulos, *J. Membrane Sci.* **2014**, *466*, 8.
[69] J. Santos, G. T. Vladisavljević, R. G. Holdich, M. M. Dragosavac, J. Muñoz, *Chem. Eng. Res. Des.* **2015**, *98*, 59.
[70] Q. Yuan, O. J. Cayre, M. Manga, R. A. Williams, S. Biggs, *Soft Matter* **2010**, *6*, 1580.
[71] K. L. Thompson, S. P. Armes, D. W. York, *Langmuir* **2011**, *27*, 2357.
[72] R. Sabouni, H. G. Gomaa, *Soft Matter* **2015**, *11*, 4507.
[73] M. S. Manga, O. J. Cayre, R. A. Williams, S. Biggs, D. W. York, *Soft Matter* **2012**, *8*, 1532.
[74] G. Sun, F. Qi, J. Wu, G. Ma, T. Ngai, *Langmuir* **2014**, *30*, 7052.
[75] F. Nan, J. Wu, F. Qi, Q. Fan, G. Ma, T. Ngai, *J. Mater. Chem. B* **2014**, *2*, 7403.
[76] R. G. Alargova, V. N. Paunov, O. D. Velev, *Langmuir* **2006**, *22*, 765.
[77] H. A. Wege, S. Kim, V. N. Paunov, Q. Zhong, O. D. Velev, *Langmuir* **2008**, *24*, 9245.
[78] T. Nallamilli, B. P. Binks, E. Mani, M. G. Basavaraj, *Langmuir* **2015**, *31*, 11200.
[79] A. Timgren, M. Rayner, P. Dejmek, D. Marku, M. Sjöö, *Food Sci. Nutr.* **2013**, *1*, 157.
[80] N. Zhang, L. Zhang, D. Sun, *Langmuir* **2015**, *31*, 4619.
[81] A. K. F. Dyab, *Colloid. Surface. A* **2012**, *402*, 2.
[82] C. P. Whitby, M. Krebsz, *Soft Matter* **2014**, *10*, 4848.
[83] C. Zhang, Y. Zhu, R. Zhang, Y. Xie, K. Wang, X. Liu, *RSC Adv.* **2015**, *5*, 90651.
[84] T. Sharma, G. S. Kumar, B. H. Chon, J. S. Sangwai, *J. Ind. Eng. Chem.* **2015**, *22*, 324.
[85] T. Fuma, M. Kawaguchi, *Colloid. Surface. A* **2015**, *465*, 168.
[86] A. Marefati, M. Rayner, A. Timgren, P. Dejmek, M. Sjöö, *Colloid. Surface. A* **2013**, *436*, 512.
[87] A. Marefati, M. Sjöö, A. Timgren, P. Dejmek, M. Rayner, *Food Hydrocolloid.* **2015**, *51*, 261.
[88] S. Ghosh, D. Rousseau, *Curr. Opin. Colloid In.* **2011**, *16*, 421.
[89] M. C. Sweedman, M. J. Tizzotti, C. Schäfer, R. G. Gilbert, *Carbohydr. Polym.* **2013**, *92*, 905.
[90] M. Sjöö, S. C. Emek, T. Hall, M. Rayner, M. Wahlgren, *J. Colloid Interf. Sci.* **2015**, *450*, 182.
[91] M. D. Rintoul, S. Torquato, *Phys. Rev. E* **1998**, *58*, 532.
[92] A. San Miguel, S. H. Behrens, *Soft Matter* **2011**, *7*, 1948.
[93] V. O. Ikem, A. Menner, A. Bismarck, *Soft Matter* **2011**, *7*, 6571.
[94] J.-W. Kim, A. Fernández-Nieves, N. Dan, A. S. Utada, M. Marquez, D. A. Weitz, *Nano Lett.* **2007**, *7*, 2876.
[95] Y. Zhao, N. Dan, Y. Pan, N. Nitin, R. V. Tikekar, *J. Food Eng.* **2013**, *118*, 421.
[96] Z. Ao, Z. Yang, J. Wang, G. Zhang, T. Ngai, *Langmuir* **2009**, *25*, 2572.
[97] A. San Miguel, J. Scrimgeour, J. E. Curtis, S. H. Behrens, *Soft Matter* **2010**, *6*, 3163.
[98] O. J. Cayre, J. Hitchcock, M. S. Manga, S. Fincham, A. Simoes, R. A. Williams, S. Biggs, *Soft Matter* **2012**, *8*, 4717.
[99] A. J. ten Tije, J. Verweij, W. J. Loos, A. Sparreboom, *Clin. Pharmacokinet.* **2003**, *42*, 665.
[100] Y.-W. Yang, C.-A. Wu, W. J. W. Morrow, *Vaccine* **2004**, *22*, 1524.
[101] S. Rebello, A. K. Asok, S. Mundayoor, M. S. Jisha, *Environ. Chem. Lett.* **2014**, *12*, 275.
[102] D. Vllasaliu, S. Shubber, R. Fowler , M. Garnett, C. Alexander, S. Stolnik, *J. Pharm. Sci-US* **2013**, *102*, 114.
[103] E. Lémery, S. Briançon, Y. Chevalier, C. Bordes, T. Oddos, A. Gohier, M.-A. Bolzinger, *Colloid. Surface. A* **2015**, *469*, 166.
[104] X. Luo, C. Li, Y. Duan, H. Zhang, D. Zhang, C. Zhang, G. Sun, X. Sun, *J. Appl. Polym. Sci.* **2016**, *133* , 43126.
[105] H. Hang, C. Li, J. Pan, L. Li, J. Dai, X. Dai, P. Yu, Y. Feng, *J. Sep. Sci.* **2013**, *36*, 3285.
[106] F. Porta, A. Kros, *Part. Part. Syst. Charact.* **2013**, *30*, 606.
[107] A. Schrade, V. Mailänder, S. Ritz, K. Landfester, U. Ziener, *Macromol. Biosci.* **2012**, *12*, 1459.
[108] N. K. Varde, D. W. Pack, *J. Control. Release* **2007**, *124*, 172.
[109] H. M. Kipen, D. L. Laskin, *Am. J. Physiol. Lung Cell. Mol. Physiol.* **2005**, *289*, L696.
[110] Z. Chen, L. Zhou, W. Bing, Z. Zhang, Z. Li, J. Ren, X. Qu, *J. Am. Chem. Soc.* **2014**, *136*, 7498.
[111] Y. Jiang, X. Liu, Y. Chen, L. Zhou, Y. He, L. Ma, J. Gao, *Bioresource Technol.* **2014**, *153*, 278.
[112] T. Sharma, N. Velmurugan, P. Patel, B. H. Chon, J. S. Sangwai, *Petrol. Sci. Technol.* **2015**, *33*, 1595.
[113] A. V. Dudchenko, J. Rolf, L. Shi, L. Olivas, W. Duan, D. Jassby, *ACS Nano* **2015**, *9*, 9930.
[114] J. Marto, L. F. Gouveia, B. G. Chiari, A. Paiva, V. Isaac, P. Pinto, P. Simõesc, A. J. Almeida, H. M. Ribeiro, *Ind. Crop. Prod.* **2016**, *80*, 93.
[115] Y. Shao, C.-H. Tang, *Food Res. Int.* **2016**, *79*, 64.
[116] D. Rousseau, *Curr. Opin. Colloid In.* **2013**, *18*, 283.
[117] H. Chen, H. Zhu, J. Hu, Y. Zhao, Q. Wang, J. Wan, Y. Yang, H. Xu, X. Yang, *ACS Nano* **2011**, *5*, 2671.
[118] S. Simovic, N. Ghouchi-Eskandar, C. A. Prestidge, *J. Drug Delivery Sci. Tech.* **2011**, *21*, 123.
[119] N. G. Eskandar, S. Simovic, C. A. Prestidge, *Curr. Drug Delivery* **2009**, *6*, 367.
[120] J. Frelichowska, M.-A. Bolzinger, J.-P. Valour, H. Mouaziz, J. Pelletier, Y. Chevalier, *Int. J. Pharmaceut.* **2009**, *368*, 7.
[121] J. Frelichowska, M.-A. Bolzinger, J. Pelletier, J.-P. Valour, Y. Chevalier, *Int. J. Pharmaceut.* **2009**, *371*, 56.
[122] L. Leclercq, V. Nardello-Rataj, *Eur. J. Pharm. Sci.* **2016**, *82*, 126.
[123] D. Marku, M. Wahlgren, M. Rayner, M. Sjöö, A. Timgren, *Int. J. Pharmaceut.* **2012**, *428*, 1.
[124] A. Cossu, M. S. Wang, A. Chaudhari, N. Nitin, *Int. J. Pharmaceut.* **2015**, *493*, 233.
[125] E. Dickinson, *Curr. Opin. Colloid Interface Sci.* **2010**, *15*, 40.
[126] E. Dickinson, *Trends Food Sci. Technol.* **2012**, *24*, 4.
[127] L. Mao, S. Miao, *Food Eng. Rev.* **2015**, *7*, 439.
[128] B. R. Shah, Y. Li, W. Jin, Y. An, L. He, Z. Li, W. Xu, B. Li, *Food Hydrocolloid.* **2016**, *52*, 369.
[129] R. V. Tikekar, Y. Pan, N. Nitin, *Food Res. Int.* **2013**, *51*, 370.

[130] P. E. Ruiz-Rodriguez, D. Meshulam, U. Lesmes, *Food Biophys.* **2014**, *9*, 406.
[131] J. Xiao, C. Li, Q. Huang, *J. Agric. Food Chem.* **2015**, *63*, 10263.
[132] C. W. Wei, J. Xia, M. Lombardo, C. Perez, B. Arnal, K. Larson-Smith, I. Pelivanov, T. Matula, L. Pozzo, M. O'Donnell, *Opt. Lett.* **2014**, *39*, 2599.
[133] B. Arnal, C. Perez, C. W. Wei, J. Xia, M. Lombardo, I. Pelivanov, T. J. Matula, L. D. Pozzo, M. O'Donnell, *Photoacoustics* **2015**, *3*, 3.
[134] B. Arnal, C. W. Wei, C. Perez, T. M. Nguyen, M. Lombardo, I. Pelivanov, L. D. Pozzo, M. O'Donnell, *Photoacoustics* **2015**, *3*, 11.
[135] T. Bollhorst, T. Grieb, A. Rosenauer, G. Fuller, M. Maas, K. Rezwan, *Chem. Mater.* **2013**, *25*, 3464.
[136] S. Li, B. A. Moosa, J. G. Croissant, N. M. Khashab, *Angew. Chem. Int. Edit.* **2015**, *54*, 6804.
[137] M. Liu, Q. Tian, Y. Li, B. You, A. Xu, Z. Deng, *Langmuir* **2015**, *31*, 4589.
[138] G. Stephenson, R. M. Parker, Y. Lan, Z. Yu, O. A. Scherman, C. Abell, *Chem. Commun.* **2014**, *50*, 7048.
[139] Q. Yuan, O. J. Cayre, S. Fujii, S. P. Armes, R. A. Williams, S. Biggs, *Langmuir* **2010**, *26*, 18408.
[140] M. Kaupp, T. Tischer, A. F. Hirschbiel, A. P. Vogt, U. Geckle, V. Trouillet, T. Hofe, M. H. Stenzel, C. Barner-Kowollik, *Macromolecules* **2013**, *46*, 6858.
[141] J.-O. You, M. Rafat, D. T. Auguste, *Langmuir* **2011**, *27*, 11282.
[142] A. J. Morse, J. Madsen, D. J. Growney, S. P. Armes, P. Mills, R. Swart, *Langmuir* **2014**, *30*, 12509.
[143] M. Wang, K. Zhang, W. Wu, J. Chen, P. Zhang, *Colloid. Surface. A* **2011**, *385*, 126.
[144] K. Zhang, W. Wu, K. Guo, J. Chen, P. Zhang, *Langmuir* **2010**, *26*, 7971.
[145] D. B. Lawrence, T. Cai, Z. Hu, M. Marquez, A. D. Dinsmore, *Langmuir* **2007**, *23*, 395.
[146] S. Zhou, J. Fan, S. S. Datta, M. Guo, X. Guo, D. A. Weitz, *Adv. Funct. Mater.* **2013**, *23*, 5925.
[147] W. Yi, H. Wu, H. Wang, Q. Du, *Langmuir* **2016**, *32*, 982.
[148] Z. Zheng, X. Zheng, H. Wang, Q. Du, *ACS Appl. Mater. Interfaces* **2013**, *5*, 7974.
[149] H.-H. Cho, H. Yang, D. J. Kang, B. J. Kim, *ACS Appl. Mater. Interfaces* **2015**, *7*, 8615.
[150] C. H. Lee, A. J. Crosby, R. C. Hayward, T. Emrick, *ACS Appl. Mater. Interfaces* **2014**, *6*, 4850.
[151] H. Yang, D. J. Kang, K. H. Ku, H.-H. Cho, C. H. Park, J. Lee, D. C. Lee, P. M. Ajayan, B. J. Kim, *ACS Macro Lett.* **2014**, *3*, 985.
[152] G. C. Phan-Quang, H. K. Lee, I. Y. Phang, X. Y. Ling, *Angew. Chem. Int. Edit.* **2015**, *127*, 9827.
[153] T. Bollhorst, S. Shahabi, K. Wörz, C. Petters, R. Dringen, M. Maas, K. Rezwan, *Angew. Chem. Int. Ed.* **2014**, *126*, 1.
[154] X. Shen, C. Xu, K. M. A. Uddin, P.-O. Larsson, L. Ye, *J. Mater. Chem. B* **2013**, *1*, 4612.
[155] N. Dan, *Curr. Opin. Colloid In.* **2012**, *17*, 141.
[156] C. Zhang, C. Hu, Y. Zhao, M. Möller, K. Yan, X. Zhu, *Langmuir* **2013**, *29*, 15457.
[157] P. H. R. Keen, N. K. H. Slater, A. F. Routh, *Langmuir* **2014**, *30*, 1939.
[158] P. H. R. Keen, N. K. H. Slater, A. F. Routh, *Langmuir* **2012**, *28*, 1169.
[159] P. H. R. Keen, N. K. H. Slater, A. F. Routh, *Langmuir* **2012**, *28*, 16007.
[160] M. Li, D. C. Green, J. L. R. Anderson, B. P. Binks, S. Mann, *Chem. Sci.* **2011**, *2*, 1739.
[161] M. Li, R. L. Harbron, J. V. M. Weaver, B. P. Binks, S. Mann, *Nat. Chem.* **2013**, *5*, 529.
[162] L. W, Z. Liao, M. Liu, X. Yin, X. Li, M. Wang, X. Lu, N. Lv, V. Singh, Z. He, H. Li, J. Zhang, *Colloid. Surface. A* **2016**, *490*, 163.
[163] N. Ballard, S. A. F. Bon, *J. Colloid Interf. Sci.* **2015**, *448*, 533.
[164] S. A. F. Bon, S. D. Mookhoek, P. J. Colver, H. R. Fischerd, S. van der Zwaag, *Eur. Polym. J.* **2007**, *43*, 4839.
[165] J. S. Sander, A. R. Studart, *Langmuir* **2013**, *29*, 15168.

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