



## Ceramic Micro-Particles Synthesised using Emulsion and Sol-Gel Technology: An Investigation into the Controlled Release of Encapsulants and the Tailoring of Micro-Particle Size

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**Abstract.** Controlled release technologies have many applications in such diverse fields as the pharmaceutical, agricultural, cosmetic and food industries, where tailored release rates and protection of the active molecule for delivery at a specific site or time are advantageous. Silica microspheres, with controlled diameters of 10–50  $\mu\text{m}$  and containing Orange II dye as a model encapsulant, have been synthesised by combining water-in-oil (w/o) emulsion technology with sol-gel chemistry. The average particle size may be controlled by the microemulsion parameters, including the surfactant and solvent concentrations, and by the sol-gel processing parameters, particularly water-to-silicon alkoxide ratio, pH, temperature, ageing and mixing conditions. Physical properties of the  $\text{SiO}_2$  microspheres, which modulate the release rates of the encapsulated molecule (including pore size and tortuosity), are also controlled by the sol-gel process parameters.

The effect of synthesis parameters, including surfactant concentration, sol-gel solution pH and drying temperature, on the morphology of the  $\text{SiO}_2$  microspheres produced will be discussed. The effect of such parameters on the corresponding release rates of the model encapsulants will also be presented.

**Keywords:** silica, sol-gel process, microspheres, emulsion, controlled release

### 1. Introduction

Controlled release technologies have many applications in the pharmaceutical [1, 2], agricultural [3], cosmetic [4] and food industries [5], where tailored release rates and protection of the active molecule for delivery at a specific site or time are advantageous. There has been considerable interest in the formation of silica particles from microemulsions [6–9]. We have developed a process combining water-in-oil (w/o) emulsion technology with sol-gel chemistry, to produce spherical  $\text{SiO}_2$  micro-particles for encapsulating and releasing active chemical compounds. A model encapsulant, Orange II dye, has been used in this study to investigate the release kinetics of the microparti-

cles. The average particle size is controlled by the emulsion parameters (including surfactant concentration, solvent concentration, and water-to-silicon alkoxide ratio), while the morphology of the microparticles is controlled by the sol-gel chemistry (i.e., pH, temperature, ageing and mixing conditions). Physical properties of the  $\text{SiO}_2$  micro-particles, which affect the release rates of the encapsulated molecule, include pore size and tortuosity. Micro-encapsulation via the combined sol-gel/emulsion process is also beneficial for protecting the active materials from a potentially aggressive environment or to prevent reactive mixing of substances until the specific target site is reached.

In this study, we have investigated the effect of initial sol-gel solution pH and drying temperature on the release kinetics of Orange II dye encapsulated within

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the microparticles. The role of emulsion chemistry in modulating the size of the particles obtained is also addressed.

## 2. Experimental Methods

### 2.1. Preparation of Silica Microspheres

A general overview of the method used to prepare microspheres in a microemulsion is given in Fig. 1. An Orange II dye solution at pH 2 was produced by dissolving 0.1 g of the sodium salt of 4-(2-hydroxy-1-naphthylazo) benzene sulfonic acid (i.e., Orange II, Sigma-Aldrich) in 10 ml of a 0.1 M nitric acid solution and diluting to 100 ml with demineralised water. A similar solution was prepared at pH 9, by adjusting the pH with aqueous ammonia instead of nitric acid. Sol-gel solutions were prepared by combining TMOS (5.21 ml, 35 mmol, Sigma-Aldrich), Orange II dye solution at the desired pH (2.52 ml, 140 mmol H<sub>2</sub>O) and methanol (140 mmol). The resulting solution was stirred for 30 min at 300 rpm and left to age for one day at ambient temperature. Sorbitan monooleate (15.08 g) was dissolved in cyclohexane (170 ml) and homogenised using a high speed blender (1200 rpm for 60 s) to form a clear surfactant solution. The sol-gel solution was then added to the surfactant solution and the resulting emulsion was stirred at 500 rpm for 1 h. A suspension of microspheres formed, which were separated from the process liquor by filtration and washed three times with cyclohexane to remove the surfactant. The resulting microspheres were then dried at room temperature for 1 day, before further drying at 60, 80 or 100°C for 3 days.

The influence of solvent and surfactant on the resulting microspheres was studied by using hexane, octane or dodecane in place of cyclohexane, and triton X-114 in place of sorbitan monooleate.

### 2.2. Analysis of Release Kinetics

The release of the dye molecule from the microspheres (0.10 g) dispersed in demineralised water (3 ml) was investigated at 25°C by monitoring the evolution of the absorbance spectra with time using a UV-visible spectrometer (Lambda 40, Perkin Elmer, USA). A fixed wavelength  $\lambda$  was used, corresponding to the absorbance maximum of Orange II in the visible spectrum ( $\lambda_{\text{max}} = 485 \text{ nm}$ ). Plots of the fraction of dye released as a function of time were obtained by dividing the actual quantity of dye released by the total mass of dye initially encapsulated in the microspheres. The total mass of dye initially encapsulated was corrected for losses during sample processing by measuring the absorbance of Orange II dye lost in the filtrate samples and wash liquors, and calculating the corresponding concentration of Orange II from an absorbance-vs.-concentration calibration curve.

### 2.3. Characterisation of Silica Microspheres

Scanning Electron Microscopy (SEM) was carried out using a Jeol JSM-6400 SEM operating at an accelerating voltage of 15 kV. Transmission Electron Micrographs (TEM) were obtained using a Jeol 2010F.

## 3. Results and Discussion

Spherical silica particles were obtained in all surfactant/solvent systems investigated, with particle size and encapsulant release rates predominantly controlled by the emulsion and sol-gel chemistry, respectively. The effects of key process parameters are discussed below.

### 3.1. Control of Encapsulant Release Rate

The effect of initial sol-gel solution pH on the release rate of Orange II dye encapsulated in microspheres

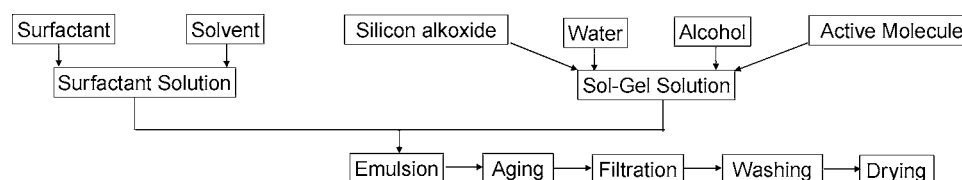


Figure 1. General method used for preparing microspheres in an emulsion.

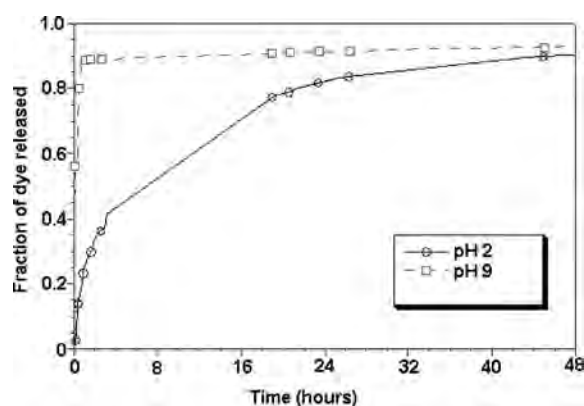


Figure 2. Influence of pH of the sol-gel solution on the release rate of Orange II dye from microspheres dried at 60°C.

prepared in the sorbitan monooleate/cyclohexane system (and dried at 60°C) is shown in Fig. 2. The results show that at pH 9 the release of Orange II dye is much faster than at pH 2. In the basic system, the majority of encapsulated dye was released within one hour. In contrast, at pH 2 the release of dye was much slower, with half of the encapsulant remaining after eight hours and sustained release observed for more than 40 h. This is a consequence of the different rates of hydrolysis and condensation in the two systems. In particular, acid catalysis promotes hydrolysis and end-of-chain condensation, leading to the formation of small, linear polymeric species [10]. During gelation, cross-linking between these linear polymers leads to the production of an open network that collapses upon drying, resulting in microporous particles with an average pore size less than 2 nm. In contrast, base catalysis promotes cross-linking and produces ramified polymers, which when coupled with dissolution-precipitation processes at high pH, leads to the formation of smooth 5–10 nm colloids. Within the “water” pools in the emulsion, these colloids aggregate to form compact gel spheres, which produce mesoporous solid spheres after drying with an average pore size in the range 2–50 nm.

The effects of drying temperatures on the release kinetics of the encapsulated dye in the silica microspheres are presented in Fig. 3. In general, an increase in the drying temperature leads to a corresponding decrease in the release rate. It is well known that solvent evaporation from nano-sized pores during drying generates significant compressive stresses, which are typically within the range 3 to 200 MPa [11]. These stresses lead to a decrease in pore size, due to densification and/or structural collapse. The observed decrease in

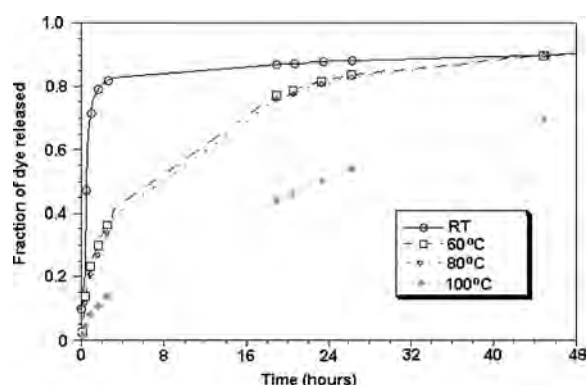


Figure 3. Effect of different drying temperatures of silica spheres, room temperature (RT), 60, 80 and 100°C, on the release kinetics of encapsulated Orange II dye.

release rates (diffusion kinetics) with increased drying temperature is thus attributed to an associated decrease in pore size. It should also be noted that the release rate can be modulated through control of such parameters as the surface fractal dimension, chemical interactions (e.g., *H*-bonding) between the oxide surface and the encapsulant, etc., although these effects will not be addressed here.

### 3.2. Control of Particle Size

The effect of solvent on the size of microspheres obtained using sorbitan monooleate as surfactant is shown in Fig. 4, while the corresponding average particle sizes are summarised in Table 1. The particle size decreases monotonically with increasing chain length in the solvent phase, while even smaller particle sizes are observed when cyclic hydrocarbons are used instead of straight-chain molecules.

Trends in particle size such as those summarised in Table 1 and Fig. 4 are often attributed to variations in the polarity of the solvent phase, as reflected in the corresponding dielectric constants [12]. Indeed, the two-fold decrease in average particle size (from 70 to 34  $\mu\text{m}$ ) that is observed when the size of the linear solvent molecules is increased from 6 to 12 carbon atoms is accompanied by a corresponding 7% reduction in dielectric constant. However, the two- to three-fold reduction in particle size (from 34 to 13  $\mu\text{m}$ ) observed when dodecane is replaced by cyclohexane is associated with an essentially negligible change in solvent dielectric constant (0.6%), suggesting that other parameters (in addition to solvent polarity) might also play a significant role in modulating particle size:

*Table 1.* Effect of solvents and surfactants on microspheres (pH 2; water-to-alkoxide mole ratio, 10).

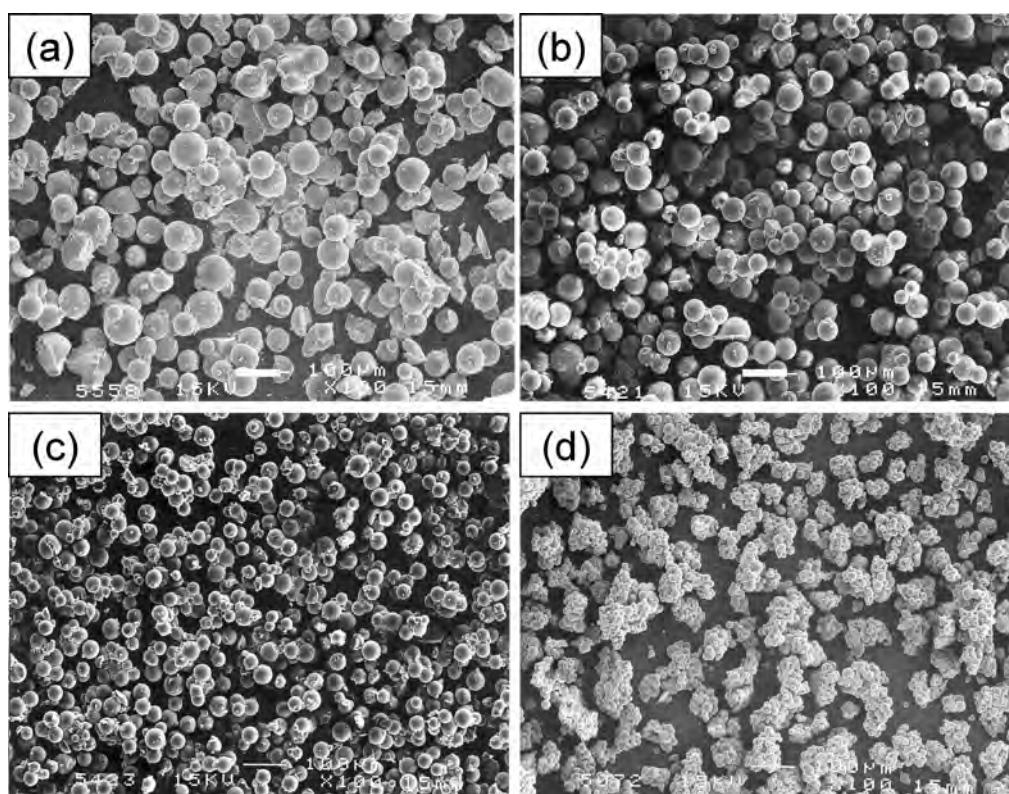
Solvent	Dielectric constant <sup>a</sup>	Interfacial surface tension (mN/m) <sup>b</sup>	Surfactant	Hydrophile-lipophile balance	Particle size ( $\mu\text{m}$ )
Hexane	1.887	50.41	Sorbitan monooleate	4.3	$70 \pm 20$
Octane	1.948	51.22	Sorbitan monooleate	4.3	$55 \pm 7$
Dodecane	2.012	Sorbitan monooleate	4.3	$34 \pm 9$	
Cyclohexane	2.024		Sorbitan monooleate	4.3	$13 \pm 9$
Cyclohexane	2.024		Triton X-114	12.4	0.25

<sup>a</sup>From Ref. [12].<sup>b</sup>From Ref. [13].

- The minimum chemical work required to form emulsion droplets is given by:

$$W_{\min} = \Delta A \times \gamma_i$$

where  $W_{\min}$  is the chemical work,  $\Delta A$  the area of the interface between the two phases (dependent on the radius,  $R$ , of the droplets) and  $\gamma_i$  the interfacial surface tension. If essentially the same energy is expended in forming all emulsions (i.e.,



*Figure 4.* SEM images showing the effect varying the solvent in the emulsion has on the size of microspheres: (a) hexane, (b) octane, (c) dodecane, and (d) cyclohexane. Scale bars, 100  $\mu\text{m}$ .

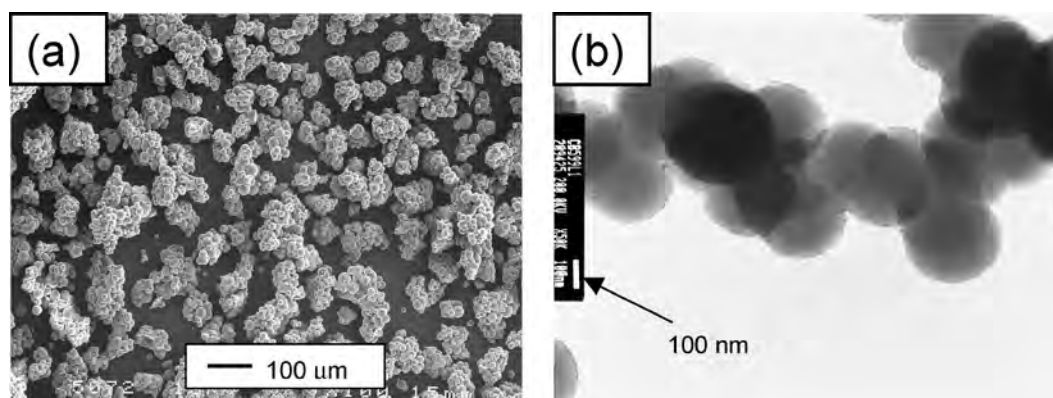


Figure 5. Influence of surfactant type on the size of spheres produced: (a) SEM image of particles synthesised using a sorbitan monooleate (span 80)/cyclohexane emulsion— $\mu\text{m}$  size range, and (b) TEM images of particles synthesised using a triton X-114/cyclohexane emulsion—nm size range.

fixed stirring rate and time), then the average surface area of the droplets would be expected to be inversely proportional to the interfacial tension (i.e.,  $1/R \propto (\gamma_i)^{0.5}$ ). Values of  $\gamma_i$  for the straight-chain hydrocarbons used in this work are included in Table 1. It is immediately evident that the variations in  $(\gamma_i)^{0.5}$  between hexane (7.10) and dodecane (7.25) are too small to account for the two-fold decrease in particle size observed when hexane is replaced by dodecane.

- It would be anticipated that the size and shape of the solvent molecules would influence the stiffness of the surfactant layer stabilising the oil-water interface in the emulsions, and hence, the rate at which colliding droplets within the emulsion exchange their contents. Relatively small solvent molecules such as hexane would penetrate readily into the surfactant layer, thus reducing its stiffness and promoting droplet exchange, leading to formation of larger particles via aggregation. Larger solvent molecules such as dodecane would not penetrate as readily into the surfactant layer, thus reducing the rate of droplet exchange and aggregation, resulting in smaller particles. This effect is even more pronounced in the case of cyclohexane, because of its relatively rigid and compact shape.

The size of the silica particles obtained via emulsion processing can also be controlled by changing such properties of the surfactant as the hydrophile-lipophile balance (HLB), which modulates the curvature at the solvent-water interface. As shown in Fig. 5,

increasing the HLB of the surfactant from 4.3 (sorbitan monooleate) to 12.4 (Triton X-114) leads to a corresponding decrease in the particle size from 13 to 0.25  $\mu\text{m}$  in cyclohexane.

#### 4. Conclusions

Combining sol-gel processing with emulsion synthesis is a powerful approach for producing inorganic particles containing encapsulated molecules, with essentially independent control of particle size and morphology. The release rate of a model encapsulant (Orange II dye) is controlled by varying the pH of the sol-gel solution, which controls the relative rates of the hydrolysis and condensation reactions mediating formation of the inorganic particles (and their pore size, volume, tortuosity, etc.). Drying conditions (time and temperature) enable the porosity of the matrix to be further tuned, providing additional tools for controlling the release rate of the encapsulated species. Acidic conditions (i.e., pH 2) in the initial sol-gel solution and higher drying temperatures of the microspheres (i.e., 100°C) result in lower release rates.

The size of the particles obtained can be readily modulated by controlling the emulsion chemistry. In particular, the average particle size decreases with an increase in the dielectric constant, steric bulk and interfacial surface tension of the solvent in the system. Similarly, increasing the hydrophile-lipophile balance of the surfactant led to a corresponding decrease in particle size.

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