COMMUNICATION

ChemComm
www.rsc.org/chemcomm

Using a liquid emulsion membrane system for the encapsulation of organic and inorganic substrates within inorganic microcapsules

Julie A. Thomas,*[a] Linda Seton,[b] Roger J. Davey[a] and Christine E. DeWolf[ac]

[a] *Department of Chemical Engineering, PO Box 88, UMIST, Manchester, UK M60 1QD. E-mail: J.Thomas@student.umist.ac.uk; roger.davey@umist.ac.uk*

[b] *School of Pharmacy and Chemistry, Liverpool John Moores University, James Parsons Building, Byrom Street, Liverpool, UK L3 3AF. E-mail: L.Seton@livjm.ac.uk*

[c] *Department of Chemistry and Biochemistry, Concordia University, 1455 De Maisonneuve Blvd. O, Montreal, Quebec, Canada H3G 1MB. E-mail: cdewolf@alcor.concordia.ca*

Received (in Cambridge, UK) 4th March 2002, Accepted 25th March 2002
First published as an Advance Article on the web 15th April 2002

We report the development of a novel technique for the encapsulation of molecular and condensed organic and inorganic substrates within hollow calcium carbonate microspheres; the process utilises precipitation at the oil–water interface of a pseudovesicular water-in-oil-in-water emulsion liquid membrane (ELM) system in order to create an inorganic shell around the pre-dispersed media.

Encapsulation is the process by which a liquid or solid active ingredient is packaged within an inert material to protect it from the surrounding environment, or conversely to protect the environment from the active ingredient. Subsequent controlled or triggered release of the encapsulated material may be achieved through control of the encapsulant porosity or changes in the external conditions. Given the numerous practical applications for micro-encapsulation such as for dyes, pharmaceuticals, agrochemicals, flavours and fragrances, the commercial possibilities connected with this methodology are numerous.[1] Most contemporary products utilise polymeric materials as encapsulants, with the encapsulation process involving complex coacervation, aqueous/organic phase separation or polycondensation processes.[2] However, considerations of biological and environmental compatibility suggest that an equivalent process designed to produce active materials encapsulated within inorganic capsules, using calcium carbonate or phosphate, might offer significant attractions. Calcium carbonate, for example, is environmentally benign and its release mechanism could be triggered by a change in pH. The phosphate, hydroxyapatite, is a key inorganic ingredient of the human body and might provide encapsulated materials suitable for pharmaceutical applications.

In this contribution we describe a novel method by which hollow vaterite microspheres can be created and used to encapsulate pre-dispersed core materials. In order to create the necessary inorganic shells we have used emulsion liquid membrane (ELM) technology to provide a unique micro-environment in which crystallisation and encapsulation can take place.[3] The size and morphology of the precipitated species can be controlled as the precipitation is confined to the dimensions of the internal water droplets of this double emulsion system.[4,5]

Based on work by Nakahara *et al.*[6] and Hirai *et al.*,[7] this method allows calcium ions, dissolved in the outer aqueous phase of a double emulsion, to diffuse across the oil membrane into the internal aqueous droplets that contain the material to be encapsulated. Carbonate ions in the internal aqueous phase react with the diffused calcium ions at the oil–water interface and solid calcium carbonate in the metastable vaterite form precipitates at the interface encapsulating any material dispersed in this phase. The vaterite spheres produced were, however, prone to transformation to the more stable calcite polymorph, a process which destroyed the capsules. In order to prevent this transformation, and stabilise the vaterite, L-glutamic acid, a known inhibitor of calcite crystallisation[8] was added to the outer aqueous phase prior to precipitation. The dried products were re-analysed by SEM after 6 months' stability trials to determine the degree of vaterite to calcite transformation and aggregation on storage. The products were found to have remained as unaggregated vaterite spheres during this storage period.

Hydrophilic polystyrene nano-particles with a diameter of 300 nm (purchased from IDC, Interfacial Dynamics Corporation), colloidal silica with a particle diameter of 40 nm (purchased from Aldrich) and dissolved acid red dye (ex. Avecia Ltd.) were chosen as candidates for encapsulation. The individual materials were pre-dispersed (and the red dye was dissolved) in the internal aqueous phase of the double emulsion by the use of a suitable surfactant (polyoxyethylene sorbitan monolaurate).[9] It is important to note that the stability of the emulsion system was unaffected by the presence of the core material to be encapsulated. In some experiments the polystyrene particles were pre-stained with 4% osmium tetroxide to facilitate detection by energy dispersive X-ray analysis.[10]

The double emulsion was prepared by mixing a solution of 3.0 M sodium carbonate, containing the material to be encapsulated, with the oil membrane phase in a 1 : 2.5 ratio at 9400 rpm for 30 min. The oil phase comprised a kerosene blend containing the surfactant mixture (sorbitan monostearate/polyoxyethylene sorbitan monolaurate, purchased from Aldrich). The two phases were mixed together until a homogeneous macro-emulsion was formed. This water-in-oil emulsion was then added to a solution of 0.2 M calcium chloride or calcium nitrate at 30 °C and the whole formulation was mixed slowly at 400 rpm. This produced the double emulsion and allowed diffusion of the calcium ion across the oil membrane. Precipitation of the vaterite spheres containing the encapsulated material was complete within 4 min. Decantation and centrifugation recovered the solid product, which was then washed with ethanol and water to remove excess oil and surfactant and then dried at 105 °C.

The products were analysed by TEM (JEOL JEM –2000 FX II transmission electron microscope), SEM (Hitachi S-520 scanning electron microscope), powder X-ray diffraction (XRD Scintag 2000 XDS), UV/Vis (Perkin Elmer Lambda 10 spectrometer) infrared (Nicolet Avatar 360 FT-IR) and Raman (LABRAM 8/128 IM spectrometer) spectroscopy.

SEM and TEM analyses provided visual evidence of the morphology, size and structure of the particles and confirmed that unaggregated microcapsules of vaterite had been produced, Fig. 1(a). The diameter of these vaterite spheres, measured from the SEM micrographs, was found to be in the range 1–12 μm. This compared well with the diameters of the internal aqueous phase emulsion droplets as measured by optical microscopy. In addition SEM and TEM, combined with integrated EDX elemental analyses, revealed, through detection of Os and Si, that polystyrene latex beads and colloidal silica particles had been encapsulated. This was further confirmed by TEM, Fig. 1(b), in which the contrast across the diameter reveals the

DOI: 10.1039/b202277j

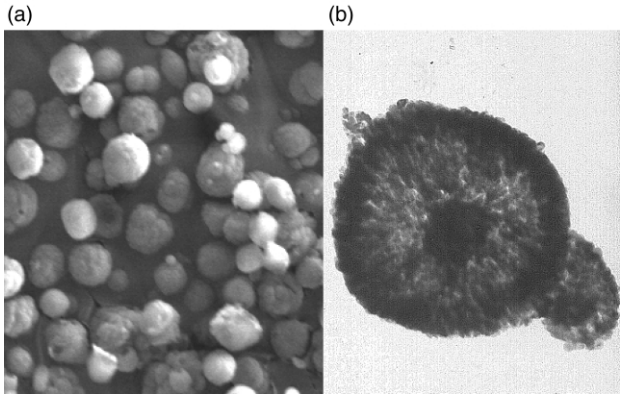

Fig. 1 (a) SEM micrograph of the unaggregated vaterite microcapsules containing polystyrene beads. (b) TEM micrograph of a vaterite sphere showing an encapsulated polystyrene bead.

thicker shell walls and the dense core of the encapsulated polystyrene. Also, no evidence was found of free polystyrene or silica particles in the products. Finally, upon acid dissolution (0.1 M HCl) of the calcium carbonate spheres the encapsulated polystyrene beads were exposed. This is observed in the SEM micrographs, Fig. 2(a) and (b).

IR and Raman spectroscopic data provided further evidence that material had been encapsulated.[11,12,13] The Raman spectrum of a group of particles showed the characteristic peaks for both vaterite and polystyrene: the stretching and bending vibrations for the C–C–H, CH_3 and C=C bonds[14] at 1610, 1450 and 1008 cm^{-1} indicated the presence of polystyrene beads while a double peak at 711 cm^{-1} confirmed vaterite.[15,16] ATR-FTIR spectra obtained on a germanium crystal with a penetration depth of 0.1 μm showed no evidence of polystyrene whereas transmission FTIR spectra, Fig. 3, showed both vaterite peaks, at 1405, 874 and 744 cm^{-1}, and polystyrene peaks, at 2987 and 1075 cm^{-1}. This again confirmed the encapsulation of the polystyrene.

UV/vis spectroscopy provided evidence for the encapsulation and triggered release of the acid red dye. Vaterite spheres with acid red dye encapsulated were dispersed in 10 mL of ethanol and the suspension centrifuged. The liquid phase was separated by decantation and the concentration of dye in the ethanol solvent was measured from its UV absorption at 550 nm. The centrifuged particles were then suspended in a mixture of hydrochloric acid (1.5 mL, 37%) and ethanol (8.5 mL). This solution, which did not require further centrifugation because the vaterite fully reacted in the acid, was then re-analysed. The concentration of dye in solution after the addition of acid increased 100-fold from 0.0002 g L^{-1} in pure ethanol, to 0.029 g L^{-1} in the presence of acid. The procedure was repeated after

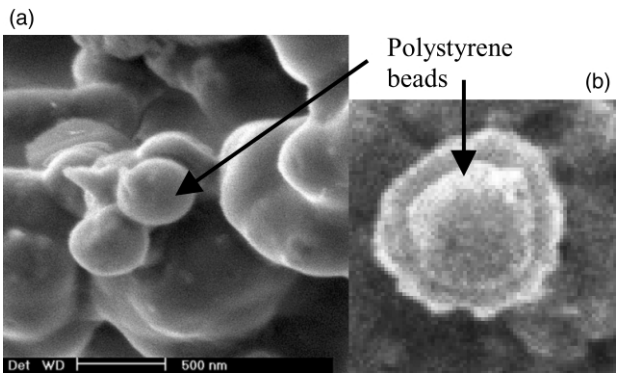

Fig. 2 (a) SEM of polystyrene beads after dissolving the vaterite spheres in (0.1 M) hydrochloric acid. (b) SEM of a polystyrene bead encased in a vaterite shell.

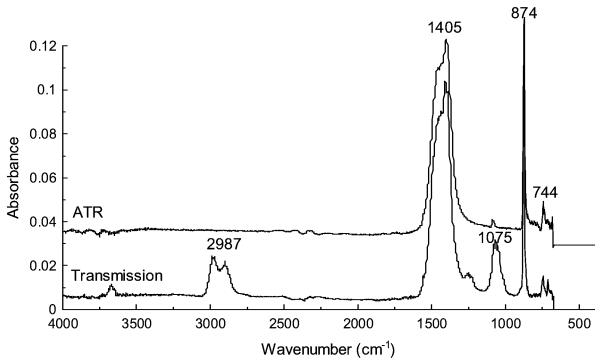

Fig. 3 Transmission infrared spectrum for vaterite encapsulated polystyrene beads compared with Atenuated Total Reflectance (ATR) infrared spectrum for vaterite encapsulated polystyrene beads.

the product had been stored in ethanol for one month. The analysis results were similar to the original experiments proving that once encapsulated the material could be retained for a prolonged period or until a trigger release mechanism was applied.

This work has demonstrated that calcium carbonate in the form of vaterite can be used to encapsulate active materials which remain stable over a prolonged period of time. Most importantly this work has demonstrated that materials of different dimensions and chemical compositions can be encapsulated and retained inside dried hollow particles with a change in pH being an effective release trigger.

It is our belief that this methodology can now be extended, not only to other solid phases but also to the encapsulation of oils or waxes by reversing the emulsion phases. From this information we conclude that such inorganic structures may have significant potential in the conventional marketplace alongside organic encapsulants.

L. S. and J. A. T. acknowledge the support of EPSRC and Avecia Ltd. through ROPA and CASE awards and the assistance of Brian Bethune, Jim Mallett and Ian Brough for TEM and SEM analyses.

Notes and references

1 C. Thies, *'Microencapsulation' Encycopaedia of Polymer Science and Engineering*, Wiley, New York–Chichester, 2nd edn., 1987, pp. 724–745.
2 A. I. Desmangles, O. Jordan and F. Marquis-Weible, *Biotechnol. Bioeng.*, 2001, **72**, 636.
3 T. Hirai, T. Hirano and I. Komasawa, *Langmuir*, 2000, **16**, 955.
4 P. J. Bruinsma, A. Y. Kim, J. Liu and S. Baskaran, *Chem. Mater.*, 1997, **9**, 2507.
5 H.-P. Lin, Y.-R. Cheng and C.-Y. Mou, *Chem. Mater.*, 1998, **10**, 3772.
6 Y. Nakahara, M. Mizuguchi and K. Miyata, *J. Colloid Interface Sci.*, 1979, **68**, 401.
7 T. Hirai, S. Hariguchi, I. Komasawa and R. J. Davey, *Langmuir*, 1997, **13**, 6650.
8 F. Manoli and E. Dalas, *J. Cryst. Growth*, 2001, **222**, 293.
9 A. Martin-Rodriguez, M. A. Cabrerizo-Vilchez and R. Hidalgo-Alvarez, *J. Colloid Interface Sci.*, 1997, **187**, 139.
10 O. Karlsson, H. Hassander and B. Wesslen, *Colloid Polym. Sci.*, 1995, **5**, 496.
11 J. Peric, M. Vucak, R. Krstulovic and D. Kralj, *Thermochim. Acta*, 1996, **277**, 175.
12 A. Flemming and A. D. Kralj, *Appl. Spectrosc.*, 1991, **45**, 1748.
13 A. G. Xyla and P. G. Koutsoukos, *J. Chem. Soc., Faraday Trans. 1*, 1989, **85**, 3165.
14 H. G. M. Edwards, D. R. Brown, J. A. Dale and S. Plant, *Vib. Spectrosc.*, 2000, **24**, 213.
15 R. W. Gauldie, S. K. Sharma and E. Volk, *Comp. Biochem. Physiol., A: Physiol.*, 1997, **118**, 753.
16 C. G. Kontoyannis and N. K. Vagenas, *Analyst*, 2000, **125**, 251.