COMMUNICATION

ChemComm
www.rsc.org/chemcomm

Shape fabrication of millimeter-sized metal-containing carboxymethyl cellulose hollow capsules

A. B. Bourlinos and D. Petridis*
Institute of Materials Science, NCSR "Demokritos", Ag. Paraskevi Attikis, Athens 15310, Greece.
E-mail: dpetrid@ims.demokritos.g

Received (in Cambridge, UK) 30th August 2002, Accepted 10th October 2002
First published as an Advance Article on the web 24th October 2002

Dropwise addition of an aqueous carboxymethyl cellulose solution to a solution of a copper or iron salt in n-butanol, leads to self-assembled, permeable millimeter sized metal-ion derivatized carboxymethyl cellulose hollow capsules of uniform dimensions and different morphologies.

Hollow capsules based on polymers, biopolymers and polyelectrolytes define a unique class of biomimetic materials that, apart from their intriguing cell type properties (artificial cells), also exhibit a wide range of applications according to their size, shape and shell permeability and composition (smart cells).[1–5] Such capsules are promising as vehicles for drug delivery and as specific reactors for the controlled encapsulation and crystallization of certain molecules and biomolecules. Hollow polymeric capsules are usually spherical and they are produced by electrostatic or covalent wrapping of colloidal spherical particles (organic or inorganic) with one or more polymeric layers followed by removal of the core-templates by dissolution or a chemical treatment.[6,7] Here we describe a novel process for the cultivation of polymer hollow capsules without the use of a core-template. Through the synergetic combination of osmotic, interfacial, co-precipitation and hydrogen bonding phenomena, the method yields spherical or disk shaped hollow capsules based on metal-ion derivatized carboxymethyl cellulose. This cellulose derivative, prepared by partial etherification of the cellulose hydroxyl groups,[8] contains metal binding carboxylate groups and a large fraction of hydroxyl groups capable of forming hydrogen bonds. The synthesis, properties and medical applications of spherical microcapsules derived from sodium cellulose sulfate and poly(diallyldimethylammonium chloride), a combination of two oppositevely charged polyelectrolytes, have been described by Dautzenberg *et al*.[9] Similarly, a polyelectrolyte membrane called Symplex, based on cellulose sulfate and polydimethylammonium chloride, has been developed.[10]

The cultivation of hollow, metal derivatized carboxymethyl cellulose capsules comprises the dropwise addition of an aqueous sodium carboxymethyl cellulose solution (2.5% w/v, 3–4 ml) to a 0.1 M $CuCl_2 \cdot 2H_2O$ or 0.1 M $FeCl_3 \cdot 6H_2O$ *n*-butanol solution (10 ml) using a dropper of 2 mm diameter. Instantly, within the organic solution spherical droplets are assembled as a result of interfacial phenomena. These droplets were allowed to age and shape for 10 min in the *n*-butanol solution by gently shaking them from time to time. During this period and as interfacial co-precipitation reactions between the carboxylate groups of the polymer and the metal ions were building up the walls of the hollow capsules, the initial transparent droplets became opaque. Subsequently, the organic solution was discarded and the flexible, shaped capsules were rinsed several times with water and finally kept in an aqueous environment in order to avoid their irreversible collapse upon drying. Similar capsules can be fabricated using aqueous solutions of Al^{3+}, La^{3+} or Cd^{2+} ions.

The morphologies and structural features of the derived capsules are shown in Fig. 1. The copper-containing carboxymethyl cellulose capsules (pale blue) are spherical in shape, hollow and with a uniform diameter (4 mm) and wall thickness (0.5 mm). On the other hand, the iron analogues (pale orange) are disk-shaped with planar and concave bases, uniform dimensions (diameter: 4 mm, thickness: 2 mm) and shell thickness (0.5 mm). Surprisingly, the morphology of the iron planted capsules is very similar to that of blood cells.[11] Concerning the size of capsules, this seems to change canonically with the diameter of the dropper, *i.e.* a dropwise addition of an aqueous polymer solution to an *n*-butanol solution of the copper salt using a dropper of half the diameter, affords hollow spheres of half size and so on. It should be pointed out that addition of an aqueous carboxymethyl cellulose solution to pure *n*-butanol did not afford shaped hollow capsules but only aqueous droplets at the bottom of the glass. Thus, controlled co-precipitation reactions at the interface, in conjunction with hydrogen bonding interactions between adjacent polymer chains, are basic factors for the stabilisation of the derived hollow structures. A crucial question is what causes the copper- and iron-planted polymeric capsules to adopt different morphologies. Since osmotic pressure has long been recognised to strongly influence many shape fabrication processes in nature, we suggest that similar phenomena are responsible for

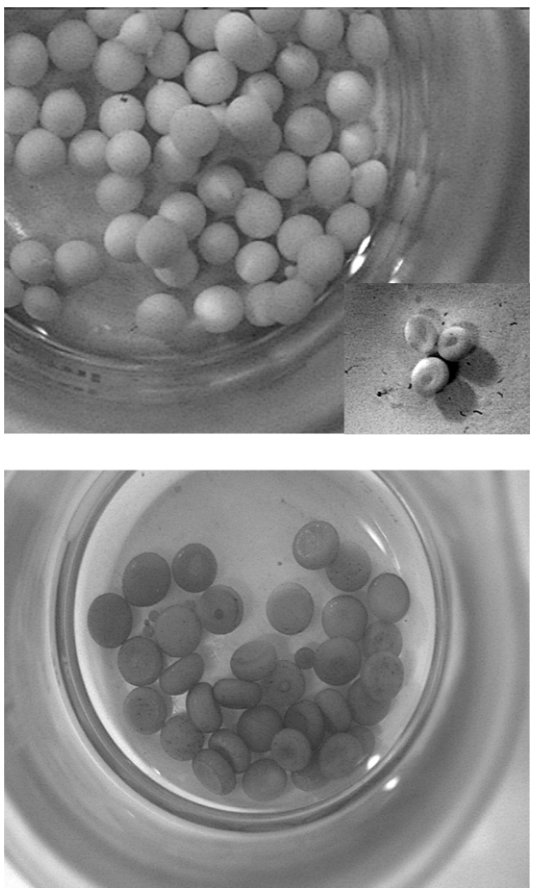

Fig. 1 Photographs of the copper (upper) and iron (lower) containing carboxymethyl cellulose capsules (the inset photo depicts the hollow structure of the corresponding capsules).

DOI: 10.1039/b208458a

the differences observed between the metal planted capsules.[12]

Another interesting aspect of the present fabrication process is the possibility of hosting other species in the hollow space of the capsules. This is achieved by dissolving or dispersing the desired guest species in the aqueous carboxymethyl cellulose solution prior to its dropwise addition to the metal-containing *n*-butanol solution. In this way, it was possible to include within the free space of the capsules water soluble molecules, such as dyes (methylene blue), as well as aqueous dispersions of powdered materials, such as nanophase particles (magnetite, tin dioxide) and porous inorganic solids (zeolite-Y, MCM-41). As an example, Fig. 2 depicts Cu^{2+}–carboxymethyl cellulose hollow spheres (in pure *n*-butanol) in the interior of which aquatic methylene blue molecules have been entrapped. The coloration developed around the spherical host capsules only a few seconds after immersion is ascribed to dye molecules which diffuse through the permeable shell of the capsules *via* osmosis and change their solvent environment from aqueous (within the capsules) to organic (outside the capsules). In contrast to methylene blue, in the case of the powdered guest materials no shell penetration was observed, since the aggregated state of the particles in their aqueous dispersion does not allow entry into the shell pores. Instead, depending on the percentage of the solid in the mother carboxymethyl cellulose aqueous solution, either the particles embrace the shell of the capsules which retain their hollow structure (small percentages, usually up to 3–5% w/v) or both functions of embracing the shell and stuffing of hollow space of the capsules are observed (percentages > 5% w/v). For example, Fig. 3 shows black–brown copper containing carboxymethyl cellulose spherical capsules stuffed with magnetite exhibiting a magnetic response in the proximity of a permanent magnet.

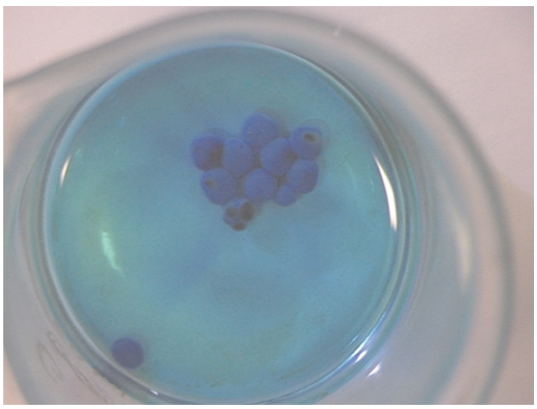

Fig. 2 The photo shows copper planted carboxymethyl cellulose spherical capsules within which methylene blue molecules have been encapsulated (the capsules are immersed in *n*-butanol). The coloration of the solvent is due to diffused dye molecules that exert the capsules thus providing evidence for their shell permeability.

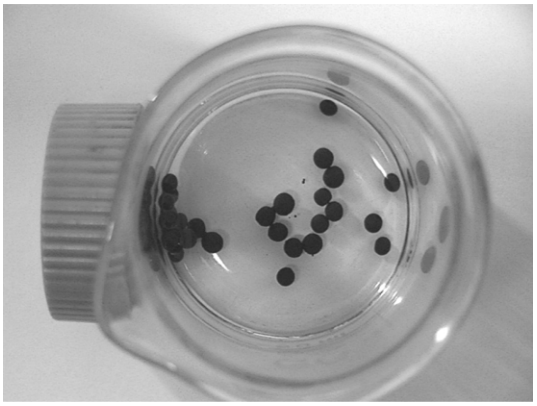

Fig. 3 Copper containing carboxymethyl cellulose capsules stuffed with magnetite attracted by a hand magnet.

In conclusion, uniform sized hollow capsules of spherical or disk-like shape, with permeable walls constructed of metal ion derivatized carboxymethyl cellulose, are easily fabricated using a novel approach based on osmotic, interfacial, co-precipitation and hydrogen bonding phenomena. The method is simple and self-consistent because it is effective without the need of core-templates, and additionally offers an easy route to encapsulation. Significantly, the same principles are equally applied for the shape fabrication of other polymers and, in principle, for the self-assembly of important biomacromolecules, such as polynucleotides (DNA) and proteins (enzymes), to hollow capsules.[13]

Notes and references

1 G. Decher, *Science*, 1997, **277**, 1232.
2 K. B. Thurmond, II, T. Kowalewski and K. L. Wooley, *J. Am. Chem. Soc.*, 1997, **119**, 6656.
3 D. E. Bergbreiter, *Angew. Chem., Int. Ed.*, 1999, **38**, 2870.
4 G. Sukhorukov, L. Dähne, J. Hartmann, E. Donath and H. Möhwald, *Adv. Mater.*, 2000, **12**, 112.
5 G. B. Sukhorukov, M. Brumen, E. Donath and H. Möhwald, *J. Phys. Chem. B*, 1999, **103**, 6434.
6 F. Caruso, *Chem. Eur. J.*, 2000, **6**, 413.
7 F. Caruso, *Adv. Mater.*, 2001, **13**, 11.
8 G. T. Austin, *Shreve's Chemical Process Industries*, McGraw-Hill, 5th edn., 1984.
9 H. Dautzenberg, U. Schuldt, G. Grasnick, P. Karle, P. Müller, M. Löhr, M. Pelegrin, M. Piechaczyk, K. V. Rombs, W. H. Günzburg, B. Salmons and R. M. Saller, *Ann. N.Y. Acad. Sci.*, 1999, **875**, 46.
10 H.-H. Schwarz, K. Richau and D. Paul, *Polym. Bull.*, 1991, **25**, 95.
11 L. Stryer, *Biochemistry*, W. H. Freeman and Company, 3rd edn., 1988, **vol. 1**.
12 F. Caruso, D. Trau, H. Möhwald and R. Renneberg, *Langmuir*, 2000, **16**, 1485.
13 For instance, dropwise addition of an aqueous sodium DNA solution (0.5% w/v) to a 0.1 M $CuCl_2 \cdot 2H_2O$ *n*-butanol or aqueous solution using a dropper of 2 mm diameter leads to uniform sized copper-derivatized DNA capsules (pale blue) 2 mm in diameter after 3–4 h aging.