Self-assembled microspheres from f-block elements and nucleoamphiphiles†

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Hollow microspheres featuring a hybrid lipid–cation multilamellar shell are prepared by hydration of a nucleoside based amphiphile with an aqueous solution containing either actinide or lanthanide salts. The physico-chemical data collected clearly indicate that the formation of these microspheres is a consequence of the following concomitant stabilizing factors: (i) hydrophobic interactions, (ii) nucleobase dimer formation and (iii) phosphate/f-block element salt binding.

Supramolecular chemistry has and continues to have a significant impact on basic research and industry.[1] Examples of supramolecular assemblies are evident in numerous biological (*e.g.*, lipids) and synthetic (*e.g.*, nanofibers) systems.[2,3] These hierarchical organizations arise as a consequence of multiple noncovalent interactions such as H-bonding, π-stacking, and electrostatics. These interactions along with metal coordination provide an efficient and powerful approach to prepare hybrid organic–inorganic assemblies having new architectures with tunable physico-chemical properties.[4] For example, supramolecular assemblies composed of f-block elements (actinides, lanthanides) are of interest for applications in photonics, catalysis, energy storage, and medicine.[5–8] Of the supramolecular assemblies prepared to date, microspheres possess a number of favorable properties for study and applications,[9,10] but to the best of our knowledge, there are no previous examples of non-polymeric microspheres constructed from amphiphiles and f-block elements. To prepare such a microsphere assembly, we exploited the unique self-organization capabilities of nucleoside-based amphiphiles and the high degrees of coordination and binding affinities of lanthanides and actinides.[11] Specifically, we report the synthesis and characterization (TEM, SEM, SAXS, ^{31}P NMR, and FTIR) of hollow microspheres composed of thorium or cerium and nucleoamphiphiles.

Nucleoside-based amphiphiles possess both the molecular recognition features present in DNA and the aggregation properties of lipids.[12] These uridine–phosphocholine amphiphiles spontaneously self-organize into supramolecular structures such as vesicles, fibers, hydrogels, and organogels.[13] In water, the nucleoamphiphiles possessing saturated alkyl chains such as DSUPC (distearoyl uridine phosphocholine, Fig. 1a), self-assemble into a hydrogel (Fig. 1b, left) in the crystalline state below their T_m (main phase temperature transition) and compact bilayers above T_m. However, in the presence of either an actinide (thorium(IV) nitrate) or a lanthanide (cerium(III) nitrate), hollow microspheres are formed. Upon hydrating the DSUPC above its T_m (T_m = 53 °C) in the presence of the f-block element salt, a white precipitate instantaneously forms (Fig. 1b, right). Scanning electronic microscopy (SEM) of the precipitates reveals microspheres, and SEM images are shown in Figs. 1c and 1d. Micron sized aggregates are observed composed of several microspheres

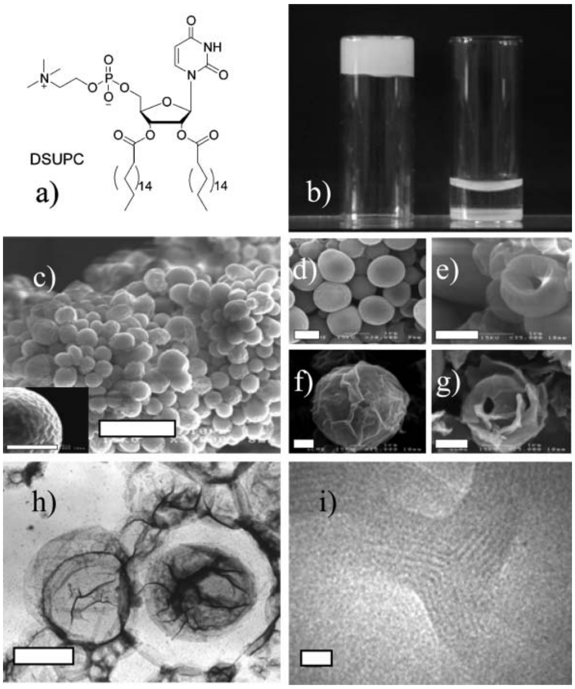

Fig. 1 (a) The structure of distearoyl uridine phosphocholine (DSUPC). (b) Samples of DSUPC in distilled water and in the presence of an f-block element salt, respectively. Left sample, a DSUPC hydrogel (5% w/w); right sample, white precipitate formed in the presence of thorium nitrate solution (500 μl, 0.16 M) upon hydration of the DSUPC (25 mg). Typical SEM images of (c), (d), (e) thorium, and (f) cerium microspheres at different magnification ((c) bar = 10 μm; (d), (e), (f) bars = 1 μm). Inset (c): magnification of a thorium microsphere surface (bar = 1 μm). (e) and (g) Images of, respectively, thorium and cerium destroyed microspheres showing their hollow structure ((g) bar = 1 μm). (h) and (i) Typical TEM images of DSUPC–f-block element microspheres ((h) bar = 3 μm, (i) bar = 20 nm).

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varying in size between 1 and 5 μm. A well-defined 3-D spherical shape is observed (Fig. 1c, inset).

Figs. 1c and 1d show thorium microspheres at different magnifications, and a cerium microsphere is shown in Fig. 1f. Similar 3-D spherical shapes are observed for both thorium and cerium. The SEM image presented in the inset of Fig. 1c, which is a magnification of a thorium microsphere, shows the outer morphology of the thorium microsphere shell. The hollow structure of these microspheres is confirmed by the partially destroyed or cracked microspheres of thorium (Fig. 1e) and cerium (Fig. 1g). Both components, nucleoamphiphile and f-block element, are required for microsphere formation. Microspheres are not formed under identical conditions when the nucleoside amphiphile or the f-block element is not present. Likewise, when a natural phospholipid (such as DSPC) which lacks the nucleoside is used instead of DSUPC, no microspheres are observed. The salt is also important since no microspheres are formed in the presence of Na^+, K^+, Ca^{2+}, Mg^{2+}, Fe^{2+} or Fe^{3+}.

These experiments also show that the microspheres are hard and robust particles, which do not collapse after drying. The persistence of the shape in the dry state can be rationalized by the stabilization of the particles *via* strong associations involving nucleoside based amphiphiles and lanthanide or actinide salts. Indeed, DSC experiments on the DSUPC in water show a T_{m} of 53.0 °C with an associated enthalpy of 0.93 kcal mol^{-1}.[13] No phase-transition is observed with the DSUPC–metal based hybrid microspheres indicating that the particles cannot be considered as a hydrated multilamellar system.

TEM images confirm the presence of hollow DSUPC–Th^{4+} microspheres (Fig. 1h).[14] The TEM images are obtained from experiments achieved without staining confirming that these objects entrapped heavy atoms in their structure. These TEM images show that the microsphere surface possesses pleats opaque to the electrons. The magnification of these pleats, appearing in Fig. 1i, indicates that the f-block element loaded microspheres exhibit multilamellar structures. To confirm the multilamellar organizations observed by TEM, small angle X-ray scattering experiments were performed on thorium loaded microcapsules. The SAXS profile shows a strong Bragg peak at $q = 1.10\ \mathrm{nm}^{-1}$ corresponding to a repeat distance of $d = 5.71$ nm. Under the same conditions, SAXS experiments achieved in the presence of cerium^{3+} exhibit a peak at $q = 1.29\ \mathrm{nm}^{-1}$, $d = 4.87$ nm.

Because this hybrid material can only be obtained in the presence of f-block element salts, we hypothesized that DSUPC–metal interactions are important in this assembly. In order to determine if the phosphate moiety of the DSUPC is involved in the stabilization of the microspheres, ^{31}P solid state magic angle spinning NMR (^{31}P MAS NMR) experiments were undertaken. The ^{31}P MAS NMR spectrum of DSUPC in the solid state shows a signal at $\delta = -1.2$ ppm. The chemical shift of the ^{31}P NMR signal undergoes an up field shift to $\delta = -12.0$ ppm in the presence thorium demonstrating that the phosphate moiety of the phosphocholine interacts with the thorium salt.[15] It is well known that the phosphatidylcholine headgroup of natural phospholipids can bind metallic cations. This type of interaction is particularly strong in the case of lanthanide and actinide cations.[16] However, in the case of natural phospholipids the complexes formed in solution are equilibrated and do not afford a definite supramolecular architecture. Simply mixing solutions of natural DSPC and thorium(IV) nitrate does not afford microspheres. Consequently, we postulated that a second stabilizing factor was involved in the formation of the solid microspheres. The nucleobase moiety on the lipid may be playing a role in the microsphere structure.

FTIR spectra were recorded on solid KBr pellets of both DSUPC and DSUPC–Th^{4+} samples in the regions 1500–2000 cm^{-1} and 2500–3700 cm^{-1}. In the case of the DSUPC–Th^{4+} mixture, a strong increase of the band at 3262 cm^{-1} corresponding to the N–H associated stretching vibration of uridine, and a decrease of the free N–H band at 3427 cm^{-1}, suggest the presence of new hydrogen bonding in the DSUPC–Th^{4+} complexes.[17] Likewise, in the presence of thorium, the additional band at 1653 cm^{-1} has been assigned to a C_4=O stretch of additional base paired uridine.[18] These results suggest that the base is also involved in the stabilization of the DSUPC–Th^{4+} hybrid microspheres *via* nucleobase dimer formation of the amphiphile.

Many of the potential applications of these microspheres require the formation of independent objects. Consequently, we developed a simple procedure for preparing separated entities. The grape-like superstructures made of microspheres can be suspended in aqueous media and sonicated for 1 min using a cleaning bath. The formation of isolated objects was observed by light and electronic microscopies. For example, the DSUPC–Th^{4+} system spontaneously forms large aggregates of microspheres (Fig. 2a), whereas single objects are clearly obtained after sonication as evident by light microscopy (Fig. 2b). As shown in Fig. 2c microspheres can also be observed by TEM after sonication. Importantly, the sonication treatment does not affect the hybrid lipid–metal microsphere shells or the average size of objects. Such a simple sonication procedure allows the preparation of individual

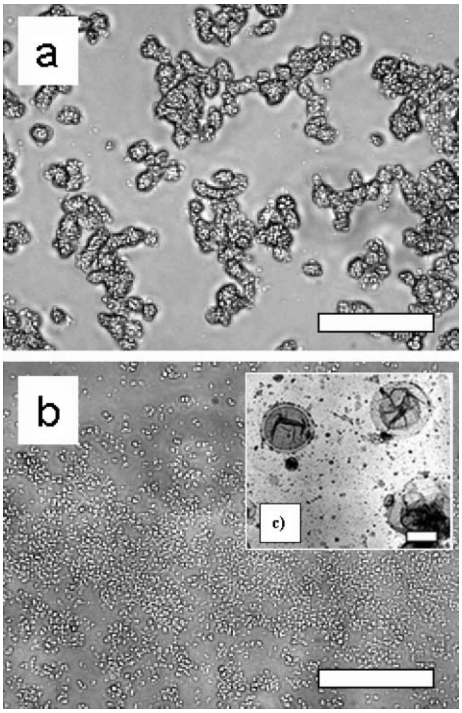
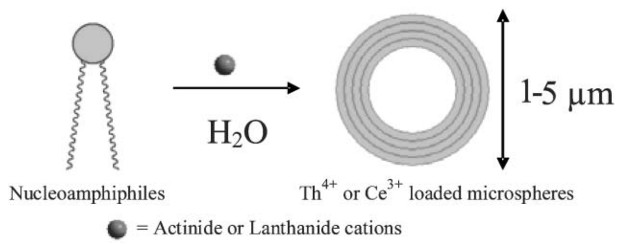


Fig. 2 Light micrographs of DSUPC–Th^{4+} microcapsules (a) before and (b) after sonication (bars = 50 μm). The grape-like superstructures of microcapsules disappear after sonication to give isolated objects suspended in solution. (c) TEM images of isolated DSUPC–Th^{4+} microspheres after sonication (bar = 2.5 μm).



Scheme 1 Proposed assembly of the hollow microspheres. Microspheres are prepared simply by hydration of a nucleoside based amphiphile with an aqueous solution containing either actinide or lanthanide salts. These objects ranging in size from 1 μm to 5 μm possess a hybrid lipid–cation shell where the cations are trapped in the multilamellar systems.

microspheres, which can be simply used as micro-objects suspended in aqueous media.

These data, collected from the physico-chemical investigations, indicate that the hybrid microsphere shells are stabilized by the following molecular interactions: (i) chain–chain hydrophobic bonding , (ii) nucleobase dimer formation and (iii) phosphate–f-block element salt binding. All these interactions are required to obtain the self-assemblies. The non-covalent hydrogen bond between uracil headgroups, phosphate–Th^{4+} and hydrophobic interactions induce association of the molecules. The resulting supramolecular assembly is a multilamellar system constituting the microspheres (Scheme 1). Finally, the aggregation of the microspheres gives grape-like superstructures, which are easily disassembled *via* sonication to provide isolated entities.

In conclusion, we have characterized microspheres prepared by hydration of nucleoside based amphiphiles with an aqueous solution containing either actinide or lanthanide salts. These actinide and/or lanthanide microspheres can be prepared as independent objects suspended in aqueous media *via* sonication. The results described herein build upon our approach of using amphiphiles with well-defined chemical and physical properties and then adding increased structural complexity to the system for creating more intricate supramolecular assemblies. The successful formation of the microspheres demonstrates the versatility and utility of this amphiphile system, highlights the importance of combining complex amphiphiles and inorganic metals to create new structures , and provides further motivation for the synthesis of nano and microscale materials using the principles of supramolecular assembly.

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