Novel fluorinated polysilsesquioxane hollow spheres: synthesis and application in drug release†

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Fluorinated polysilsesquioxane (FPSQ) hollow spheres with a large empty interior were synthesized in an aqueous medium by using (trifluoropropyl)trimethoxysilane as the sole precursor. The drug release applications of these spheres were demonstrated, and the materials have great potential as fluorinated drug release carriers.

Hollow micro/nanostructured materials have attracted increasing interest for their potential applications as nanoparticle collectors, efficient catalysts, and drug-delivery carriers because of their empty interior. These materials include both organic hollow materials, such as polymer capsules, and inorganic hollow materials, such as one-dimensional nanotubes or silica hollow spheres. However, very few studies have examined organic–inorganic hybrid materials with hollow structures. Hah et al. investigated phenyl-functionalized hollow polysilsesquioxane (PSQ) particles, and Yuan et al. prepared thiol-functionalized hollow polysilsesquioxane spheres with a general formula of [RSiO1.5]n, where R is an organic group. Regardless of the hollow structure, some polysilsesquioxane hard spheres, with functional groups including mercapto, amine, vinyl, acrylic or isocyanate, have been synthesized. This type of organic–inorganic molecular-level hybrid polymers has many unique properties, which traditional composite materials do not exhibit.

Fluorinated functional materials exhibit satisfactory performances in the fields of sensing, catalysts, biology and environmental protection thanks to their unique properties, such as low surface energy, high contact angle, reduced coefficients of friction, and hydrophobicity. In particular, fluorinated silicon-based materials are useful in many applications because of the unusual chemical and physical properties that are imparted by fluorine for these organic–inorganic nanocomposites. Some studies have shown that the introduction of fluorine onto silica can meet versatile requirements. Johnston and co-workers grafted perfluorodecane side chains onto silica surfaces and successfully stabilized a nontilute silica dispersion in liquid carbon dioxide at 25 °C and at the vapor pressure. Otsuka et al. used a fluorocarbon modified silica as a drug carrier to improve the drug recovery efficiency from phytonadione-loaded silica gels. Nie’s group used (trifluoropropyl)trimethoxysilane (TFPTES)/tetraethyl orthosilicate (TEOS) mixed precursors to prepare fluorine-modified silica membranes with a high hydrothermal stability for hydrogen separation. However, the post-modification of silica usually requires more complicated processing steps, such as additional coupling reactions under heating, and obtaining monodispersed particles is difficult due to aggregation, whereas TFPTES/TEOS mixed precursors lead to a limited fluorine-content in the materials.

The amount of functional groups on the surfaces of hollow structured materials directly affects the materials’ properties and applications. Until now, the synthesis of fluorinated polysilsesquioxane hollow spheres with a high surface coverage still remains a challenge.

In this communication, fluorinated polysilsesquioxane hollow spheres were prepared for the first time, and their applicability in drug release systems was demonstrated. The FPSQ hollow spheres were synthesized directly via the hydrolytic polycondensation in aqueous solution. The hollow spheres not only had a high surface coverage of the fluoroalkyl group (theoretically, 6.71 mmol g−1), but also had a typical particle size of 192 ± 12 nm, which is quite suitable for many applications, especially for controlled drug release systems. An example of the drug release was demonstrated using these FPSQ hollow spheres as the drug carrier. The in vitro drug release studies demonstrated that a steady release process was obtained for the fluorinated drug using this carrier.

The fabrication procedure consists of two steps: the synthesis of a polystyrene (PS) template and the growth of the polysilsesquioxane shell on the polymer surface as shown in Scheme 1 (see the ESI† for the detailed procedure). In the first step, polyvinylpyrrolidone (PVP)-modified PS beads were prepared through an emulsifier-free emulsion polymerization in an aqueous medium. The scanning electron microscopy observations (Fig. 1a) demonstrated that the as-prepared PS spheres had an approximate size of 140 ± 10 nm, with a very narrow distribution. In the second step, different amounts (0.5 to 4.5 mL) of ammonia were added into the PS suspension, and then the (3,3,3-trifluoropropyl)trimethoxysilane (FTMS) precursor was added very slowly dropwise into the mixture. The fluorinated polysilsesquioxane shell grew on the PS surface through a hydrolytic condensation process. As shown in the SEM images and DLS data (Fig. 1b–f), the as-prepared products maintained a spherical morphology with an average diameter of around 200 nm in a narrow size distribution.

Scheme 1 Preparation of the fluorinated polysilsesquioxane hollow spheres and their application in a drug release process.

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The formation of the fluorinated polysilsesquioxane hollow spheres relies on the hydrolysis and polycondensation reactions. It is generally considered that the silsesquioxanes tend to form three Si–O–Si bonds, and the cyclization reactions play an important role in the polymerization process, which result in the polysilsesquioxanes containing cage-like structure.25,26 On the other hand, the uncontrolled hydrolysis of organosilica precursor with excess of water could finally produce some random network macromolecule in the system. Just as shown in the IR spectrum (Fig. 3a), the strong absorption peaks at 1132 cm\(^{-1}\) and 1070 cm\(^{-1}\), indicated by arrows, represent the cage-like and the network structure, respectively.27 Fig. 3b displays the XRD pattern with two halos at 8.6° (\(d = 1.03\) nm) and 20.6° (\(d = 0.43\) nm) which was thought to be related to the ladder-like double chain.28 Based on the above discussion, it seems that the fluorinated polysilsesquioxanes may be composed of a mixture of cage-like, random network and ladder-like structures.

Two types of fluorinated drugs (5-fluorouracil (5-FU), flucytosine) and one type of non-fluorinated drug (captopril) were loaded as the model molecules in order to investigate the capability of the FPSQ hollow spheres as drug carriers. The FPSQ hollow spheres were immersed in an aqueous drug solution with vigorous stirring to make sure the drugs diffused into the carriers. The release experiments were performed in 30 mL of a PBS solution at pH 7.4 and 37 °C (Fig. 4). During these experiments, 11% 5-FU and 27% flucytosine were released in 1 h. However, for captopril, about 81% of the drug was released in one hour. The profiles also showed that an initial fast release was observed when non-fluorinated drug was loaded, while a slow release when the fluorinated drug was loaded, although the mechanism is still being studied.
In summary, new fluorinated polysilsesquioxane hollow spheres were prepared and used for drug release. The monodispersed FPSQ hollow spheres had a high fluoroalkyl coverage surface and an empty interior, providing these materials with some potential applications, such as catalysts, gas separation, coating materials, nanoreactors and so on. The in vitro drug release experiments demonstrated that the hollow FPSQ spheres could potentially be applied as release carriers for fluorinated drugs.

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Notes and references