Multifunctional halloysite nanotubes for drug delivery and magnetic resonance imaging

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Introduction: Halloysite is aluminosilicate clay which has hollow tubular structure, with the alumina lining for the lumen wall and silica as the outer layer. Halloysite clay as a new type of nanocarrier has been used for various applications, including nanocontainer for loading and controlled release of active agents (such as drugs, proteins, etc.), anticorrosion or protection (1). Superparamagnetic iron oxide (SPIO) nanocrystals are effective MRI agents used for molecular imaging. The SPIO nanocrystals which have good control over size and crystal structures in organic solvent need to be transferred into aqueous phase and further used for biomedical applications. Layer-by-layer (LbL) self-assembly has been a successful technique to develop advanced functional materials with finely tuned molecular architecture.

In this work, SPIO nanoparticles and proteins are incorporated in halloysite nanotube systems through LbL self-assembly for both imaging and drug delivery applications.

Methods:

Reagents: Halloysite clay tube samples were obtained from Applied Minerials Inc. Poly (styrenesulfonate) (PSS, MW: 70kD), Poly(allylamine) hydrochloride (PAH, MW: 56K), were purchased from Aldrich Chemical Co..

N-alkyl-PEI2k Stabilized SPIO Nanocomposites: SPIO nanoparticles were prepared by the method described in previous publication by Sun et al. (2). SPIO nanocrystals in hexane were dried under argon and redispersed in chloroform together with alkylated PEI2k. Then, mixed solution was slowly added into water with sonication. The mixture was under shaking for overnight to remove chloroform (3).

Protein Loading Into Halloysite Nanotubes.
Embedding BSA to carrier systems was conducted by mixing halloysite dry powders with BSA solution in water, and then vacuumed to exclusion the air inside the lumens of nanotubes. Finally, the tubes were rinsed completely with Milli-Q water.

Self-Assembly of Polyelectrolyte Films on Halloysite and Doping of N-alkyl-PEI2k nanocomposites.
Halloysite nanotubes loaded with BSA were coated by two bilayers of PAH/PSS through LbL self-assembly, and positively charged SPIO nanocomposites were adsorbed through electrostatic adsorption.

Results: The BSA loading capacity was tested by TG analysis at a heating rate of 10 deg/min (Fig. 1, d). From the TG result, we found that BSA raw materials had the major mass loss of 67.5% from 180 to 800 degrees, and halloysite was about 14.9% (I). The BSA loaded halloysite with one time washing (IV) displayed 23.71% mass loss, with approximately 17.1% attributed to the BSA incineration. In comparison, three times washings (II) led to lower mass loss (21.0%), probably because of removal of BSA adsorbed on the nanotubes' surface. SEM image shows that the surface of halloysite/BSA nanotubes after 3 times washing (c) having much

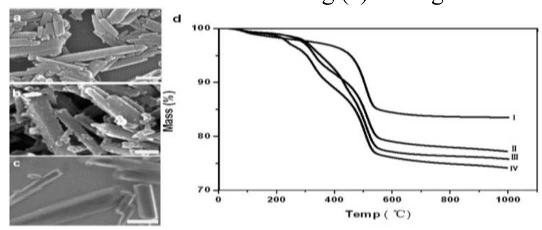

Figure1. Scanning electron microscope (SEM) images of halloysite material (a), halloysite/BSA after 1 time washing(b) and 3 times washing(c) (scar bar = 200 nm), TG curves (d) of halloysite material (I), halloysite/BSA after 1 time washing (IV) and 3 times washing (II), halloysite/BSA-(PAH/PSS)$_2$ (III).

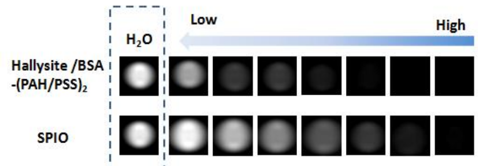

Fig. 2. T2-weighted MRI images (1.5 T, TR = 5000 ms, TE= 25 ms) of SPIO-N-alkyl-PEI2k nanocomposites and clay-(PAH/PSS)$_2$-SPIO nanotubes. Fe concentration: 0.03mM, 0.06mM, 0.1mM, 0.15mM, 0.2mM, 0.3mM, 0.4mM, 0.5Mm.

smoother surface than the one time washed ones (b). After coating of two PAH/PSS bilayers on nanotubes' surface, the mass loss slightly increased to 22.59% (III), mainly caused by the absorption of polyelectrolytes.

To evaluate the effect of halloysite/SPIO nanocomposites in MRI imaging, nanotubes are tested under a 1.5T MRI scanner. The MRI signal intensity was compared between halloysite/SPIO nanotubes and SPIO-N-alkyl-PEI2k nanocomposites (Fig. 2). For a given Fe concentration, halloysite/SPIO nanotubes display hypointense images than those containing just a single particle, confirming that SPIO doping increases image contrast.

Conclusions: BSA was loaded into halloysite nanotubes successfully and the polyelectrolyte/magnetite multilayer thin films were constructed via LbL self-assembly technique. The nanotubes doped with SPIO nanocomposites have better image contrast comparing to single SPIO nanoparticles. This novel composite nanotube may be used as MRI visible drug carriers for biomedical applications.

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