Electronic Supplementary Information

Trivalent Galactosyl-Functionalized Mesoporous Silica Nanoparticles as a Target-Specific Delivery System for Boron Neutron Capture Therapy

Chian-Hui Lai,[a] Nien-Chu Lai,[a] Yung-Jen Chuang,[b] Fong-In Chou,[c] Chia-Min Yang*[a] and Chun- Cheng Lin*[a]

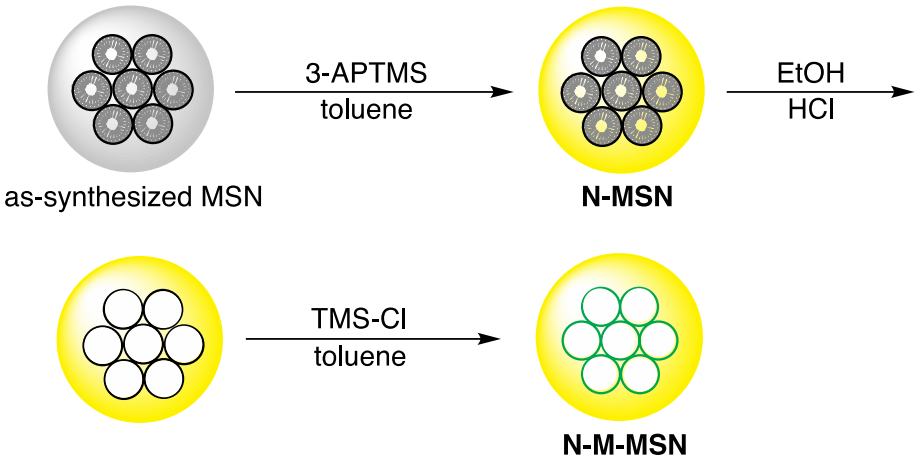
[a] *Department of Chemistry, National Tsing Hua University 101, Sec. 2, Kuang-Fu Rd., Hsinchu 30013, Taiwan (R.O.C.). E-mail: cclin66@mx.nthu.edu.tw; cmyang@mx.nthu.edu.tw*
[b] *Department of Medical Science and Institute of Bioinformatics and Struc- tural Biology, National Tsing Hua University 101, Sec. 2, Kuang-Fu Rd., Hsinchu 30013, Taiwan (R.O.C.).*
[c] *Department of Nuclear Science and Technology Development Center, Na- tional Tsing Hua University 101, Sec. 2, Kuang-Fu Rd., Hsinchu 30013, Taiwan (R.O.C.).*

Content:

I. Preparation of the bifunctional MSNs (N-M-MSN)

As shown in Shceme S1, the preparation of bifunctional MSNs started from the synthesis of pure-silica MSNs. A solution of hexadecyltrimethylammonium bromide (122 mg, Acros) in water (576 mL) was mixed with NaOH solution (0.4M, 16.2 mL) and ethanol (17.1 mL, Merck). Tetraethylorthosilicate was then added into the solution, and the mixture was stirred for 2 h and then aged at 90 °C for 48 h. The product was washed, filtered, and dried in air. For the functionalization of the external surface, the as-synthesized sample (0.5 g) was dried at 80 °C for 12 h in vacuum and was then poured in a solution of toluene (50 mL, Echo) and 3-APTMS (5 mL, 95%, Acros) and stirred at 80 °C for 24 h in an argon atmosphere. The product, designated as **N-MSN**, was washed with toluene and ethanol and dried in air. The surfactant molecules in **N-MSN** were removed by repeated extraction with acidified ethanol. The surfactant-free sample (0.1 g) was again suspended in a solution of toluene (5.0 mL) and trimethylchlorosilane (0.6 mL, 98%, Gelest) and the mixture was stirred at 30 °C for 15 min. The resulting sample, designated as **N-M-MSN**, was washed with toluene and ethanol and dried in air. As shown in Scheme S1, the preparation of bifunctional MSNs began with the synthesis of pure silica MSNs. A solution of hexadecyltrimethylammonium bromide (122 mg, Acros) in water (576 mL) was mixed with NaOH (0.4 M, 16.2 mL) and ethanol (17.1 mL, Merck). Tetraethylorthosilicate was then added to the solution, and the mixture was stirred for 2 h and then aged at 90 °C for 48 h. The product was washed, filtered, and dried in air. To functionalize the external surfaces, the initially synthesized sample (0.5 g) was dried at 80 °C for 12 h in vacuum and was then poured into a solution of toluene (50 mL, Echo) and 3-APTMS (5 mL, 95%, Acros) and stirred at 80 °C for 24 h in an argon atmosphere. The product, designated as **N-MSN**, was washed with toluene and ethanol and dried in air. The surfactant molecules in **N-MSN** were removed by repeated extraction with acidified ethanol. The surfactant-free sample (0.1 g) was again suspended in a solution of toluene (5.0 mL) and trimethylchlorosilane (0.6 mL, 98%, Gelest), and the mixture was stirred at 30 °C for 15 min. The resulting sample, designated as **N-M-MSN**, was washed with toluene and ethanol and dried in air.

II. Supplementary scheme and figures



Scheme S1. Preparation of the bifunctional sample, **N-M-MSN,** which has amino functionality on the external surfaces and hydrophobic methyl groups on the mesopores.

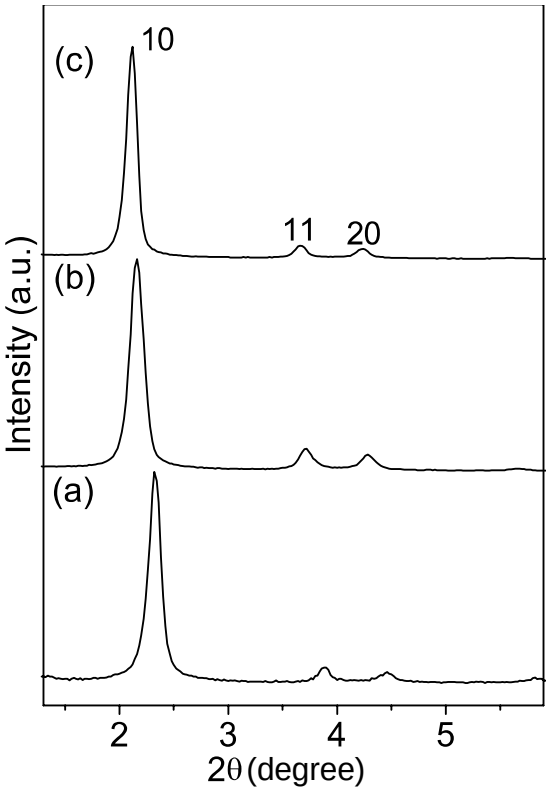


Fig. S1. Powder XRD patterns of (a) the initially synthesized MSNs, (b) N-MSN, and (c) N-M-MSN.

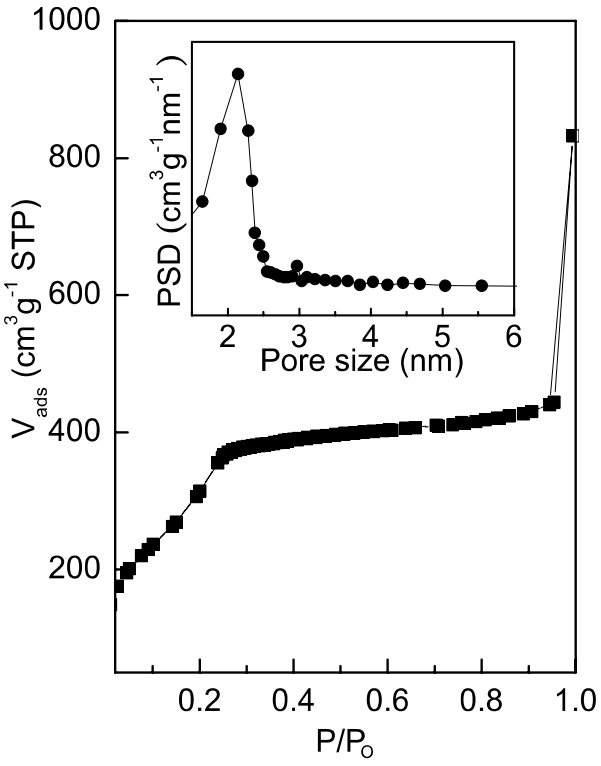


Fig. S2. Nitrogen physisorption isotherms at 77 K and an inert figure corresponding to the pore size distribution of N-M-MSN.

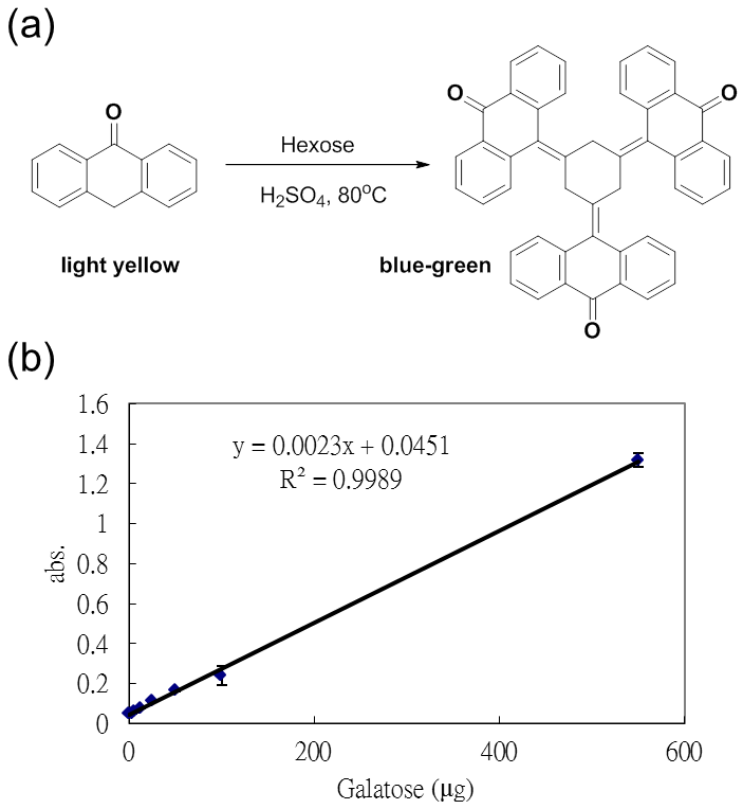


Fig. S3. (a) The product of an anthrone-sulfuric acid carbohydrate colorimetric assay and (b) a standard curve for galactose quantification.

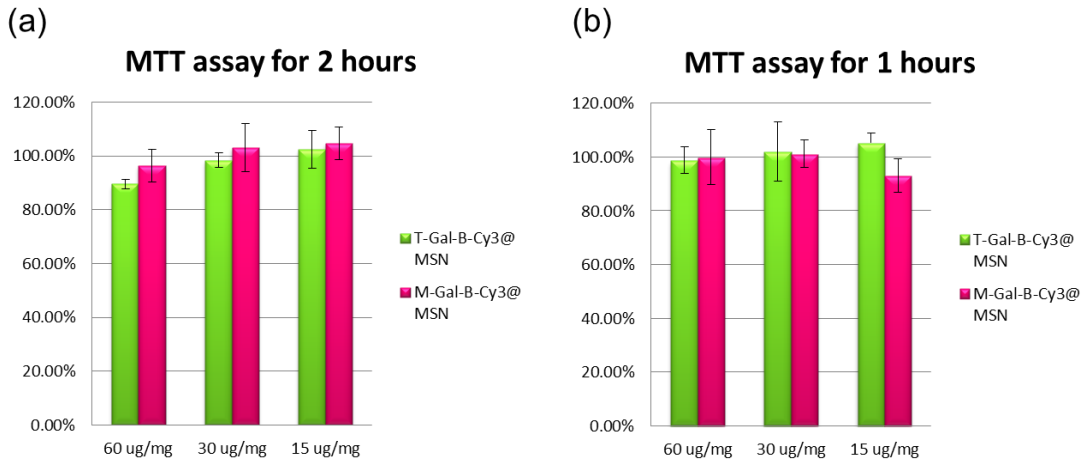


Fig. S4. Cytotoxicity of **T-Gal-B-Cy3@MSN** and **M-Gal-B-Cy3@MSN**, determined by an MTT assay. None of the MSNs showed cytotoxic effects on HepG2 cells after 1 h or 2 h.