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Supporting Information for

Multifunctional Hybrid Aerogels: Hyperbranched Polymer-Trapped Mesoporous Silica Nanoparticles for Sustained and Prolonged Drug Release

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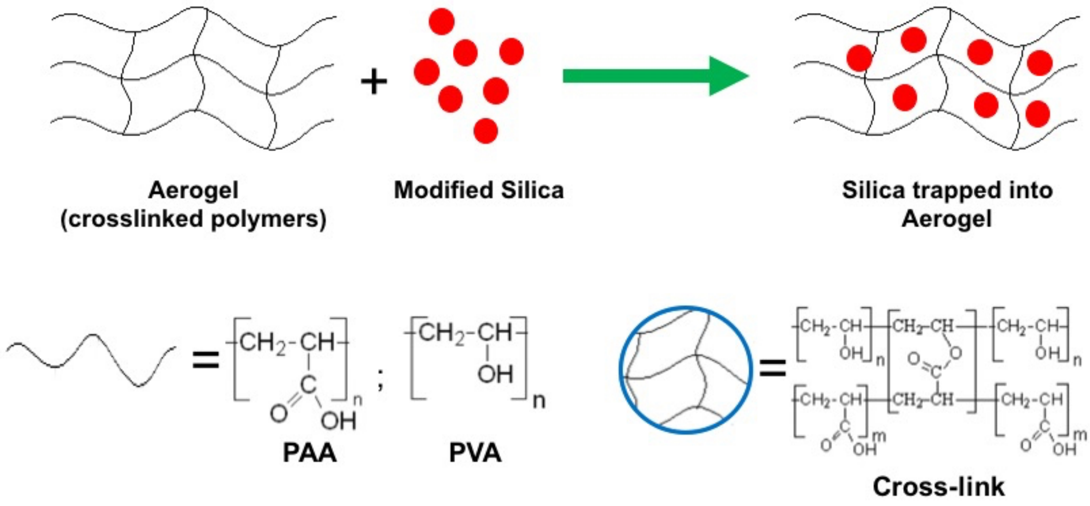
Additional Experimental Section and Results

Synthesis of SBA-15 mesoporous silica nanoparticles and their surface functionalization

First Pluronic 123 (4 g) was dissolved in a solution containing concentrated HCl (37 %) (24 mL) and distilled water (104 mL). After adjusting the temperature of the solution at 45 °C, TEOS (8.5 g) was added into the solution. The solution was then vigorously stirred for 24 h, and after which, it was kept in oven at 80 °C for 24 h. The as-prepared mesostructured SBA-15 nanoparticles were recovered by filtration, washed copiously with distilled water, and then dried in oven at 40 °C. Prior to template extraction, the external surface of the as-prepared mesostructured SBA-15 nanoparticles were modified with quaternary ammonium groups by stirring 300 mg of the sample in TOSPTA/toluene (1 mL/150 mL) solution for 6 h at 80 °C. The mesostructured SBA-15 nanoparticles whose external surfaces were capped with quaternary ammonium groups were stirred in a solution (100 mL) of diethyl ether:ethanol (1:1 ratio) for 24 h to remove the Pluronic 123 template and to create the channel pores. The resulting mesoporous SBA-15 nanoparticles were then stirred in a solution of hexamethyldisilazane (HMDS) (1.5 mL) in either anhydrous toluene or 2-propanol (30 mL) for 2 h at 60 °C to graft methyl groups onto their channel walls. The solid products were recovered by filtration, washed with copious amount of ethanol, and dried in oven at 40 °C. The resulting two different SBA-15 mesoporous silica nanoparticles whose external surfaces were capped with quaternary ammonium groups and whose internal surfaces were modified with higher or lower density of methyl groups were labeled as SPH-4 and SPH-4L, respectively.

Additional Results

The formation of cross-linkages in the polymers (Scheme 1) was characterized using Fourier transform infrared (FTIR) spectroscopy. To differentiate the carboxylic acid groups from the esters groups formed by the solid-state reaction, which can have overlapping peaks on FTIR spectra, the aerogels were treated with a basic solution to convert the remaining carboxylic acid into carboxylate groups by putting the SPH aerogels in a flask containing 30 mL of aqueous 0.1 M NaOH solution at room temperature for 30 min and then taking them out of the solution and letting them dry under ambient condition.



Scheme S1. Schematic representation of aerogel structure.

The FTIR spectra of the SPH-1 before and after treatment with NaOH solution are presented in Figure S1. The spectra show some features that are common in all the cases (Figure S2). For instance, a broad band at *ca*. 3480 cm^{-1} due to O-H stretching, a band at *ca*. 2940 cm^{-1} attributable to the C-H stretching vibration of CH_2 groups from both polymers, and the band at 1240 cm^{-1} due to the O-H bending vibration were observed. However, the region between 1750 to 1500 cm^{-1}, where the C=O stretching bands typically appear and which is important to confirm formation of cross-linked bonds between PVA and PAA through a solid-state reaction, was particularly monitored. In the spectra of samples before being subjected to treatment with basic solution, a single peak at 1720 cm^{-1} associated with carbonyl groups is observed. In the spectra of the sample after treatment with a dilute basic solution though, it was possible to see the change in the peaks in the carbonyl region or the appearance of an intense band at 1567 cm^{-1} that is attributed to C=O stretching of carboxylate groups. More importantly, after the treatment with a base, the peak at 1720 cm^{-1} was not completely vanished. Consequently, the remaining peak at 1720 cm^{-1}, after the samples are kept in 0.1 mol/L NaOH solution for 30 min, was due to the carbonyl moiety of ester groups formed in the cross-linking reaction.

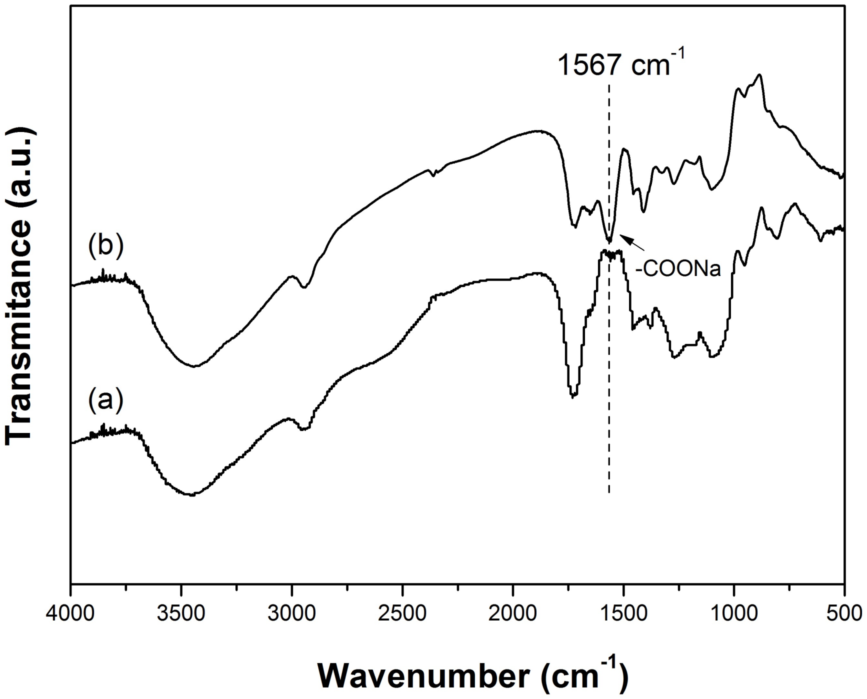


Figure S1. FTIR spectrum of SPH-1 aerogel: before (a) and after (b) immersing the material into aqueous NaOH solution (0.1 M) and then taking it out of the solution and letting it to dry under ambient condition.

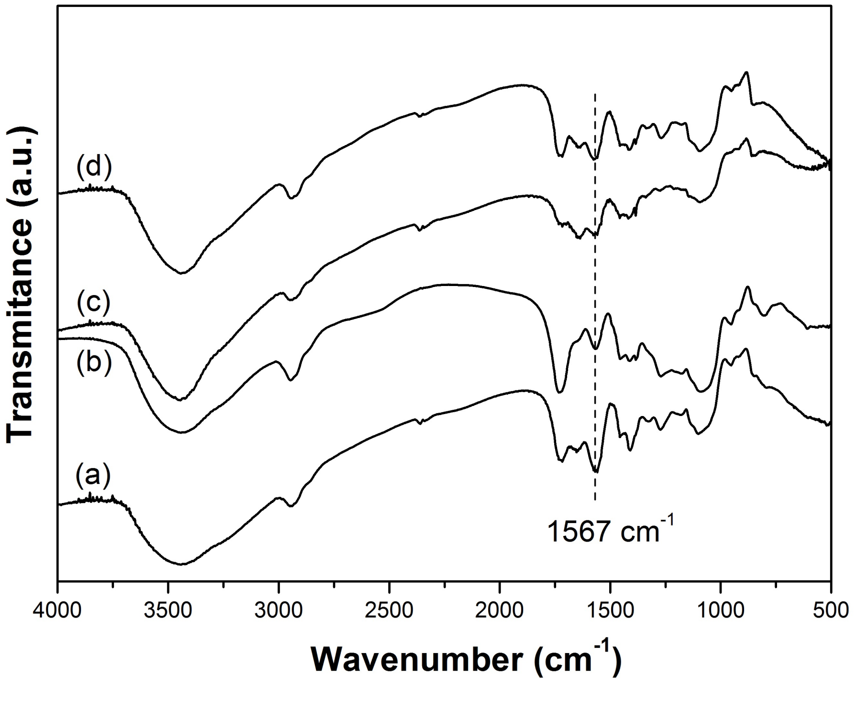


Figure S2. FTIR spectra of SPH-1 (a), SPH-2 (b), SPH-3 (c), and SPH-4 (d) aerogels after being immersed in aqueous NaOH solution (0.1 M) and then taking them out of the solution and letting them dry under ambient condition.

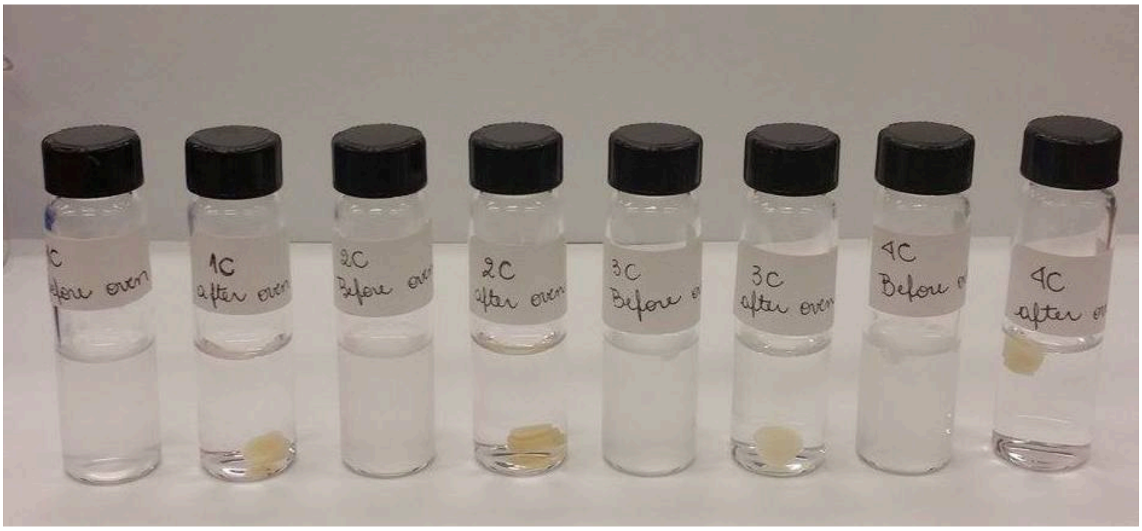


Figure S3. Different SPH aerogels dipped into aqueous NaOH solutions (0.1 M). The sample labels go in accordance with those described in Table 1; for example, sample 1C (the second one in the image) corresponds to SPH-1 aerogel, and so on.

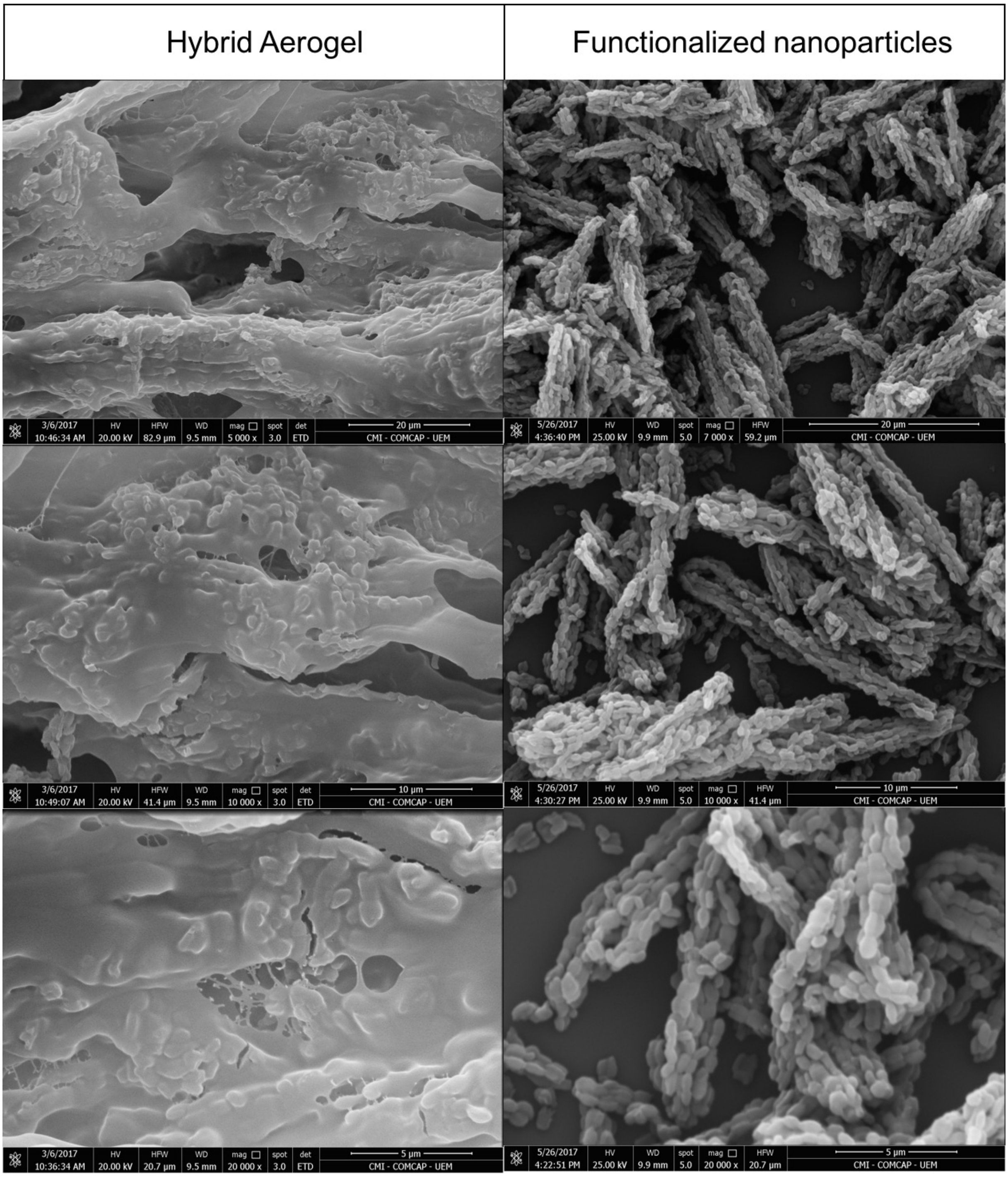


Figure S4. (Left panels) SEM images of SPH-1 hybrid aerogel. (Right panels) SEM images of methyl-functionalized SBA-15 mesoporous silica nanoparticles.

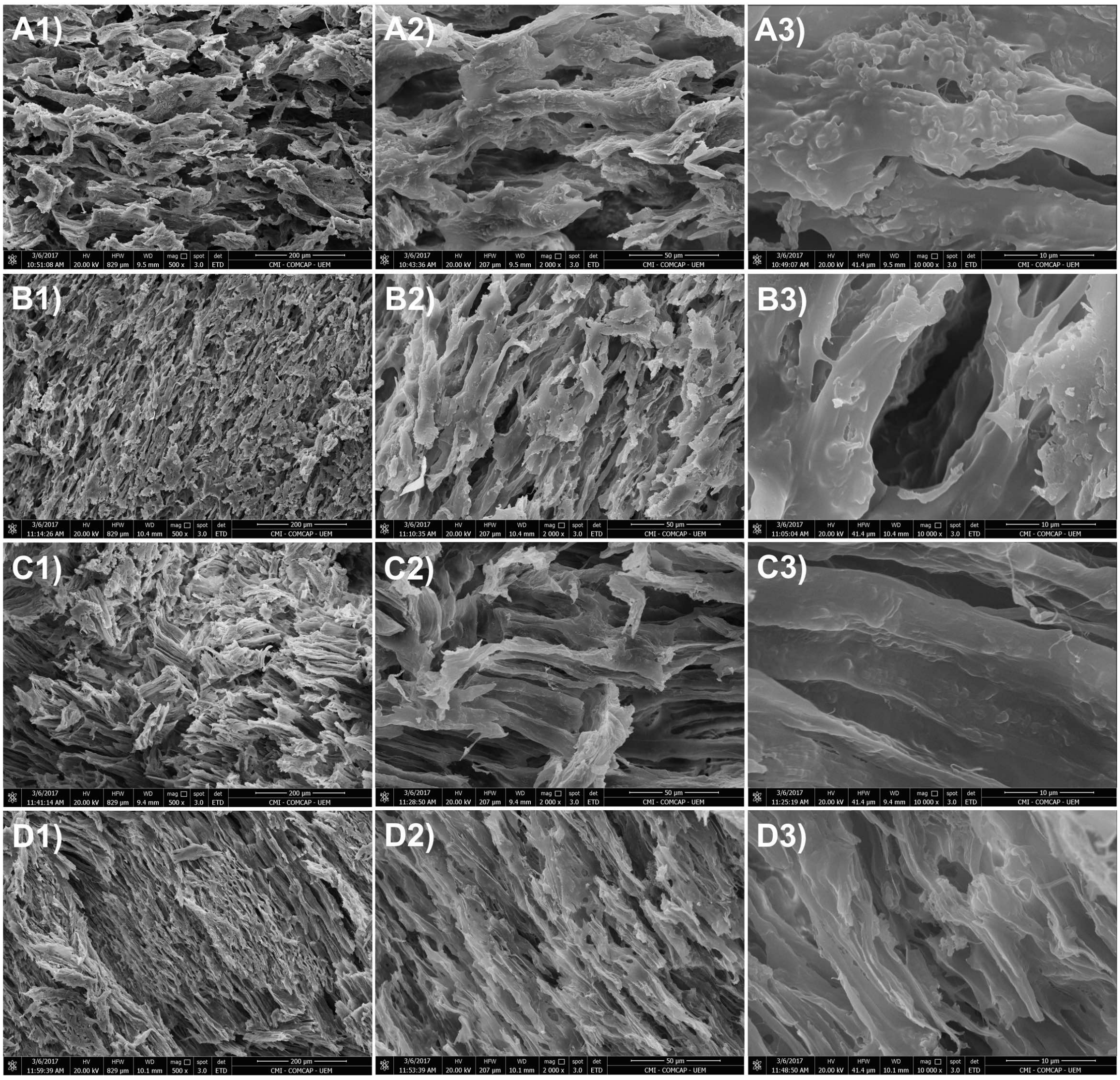


Figure S5. SEM images of SPH-1 (A), SPH-2 (B), SPH-3 (C), and SPH-4 (D) aerogels.

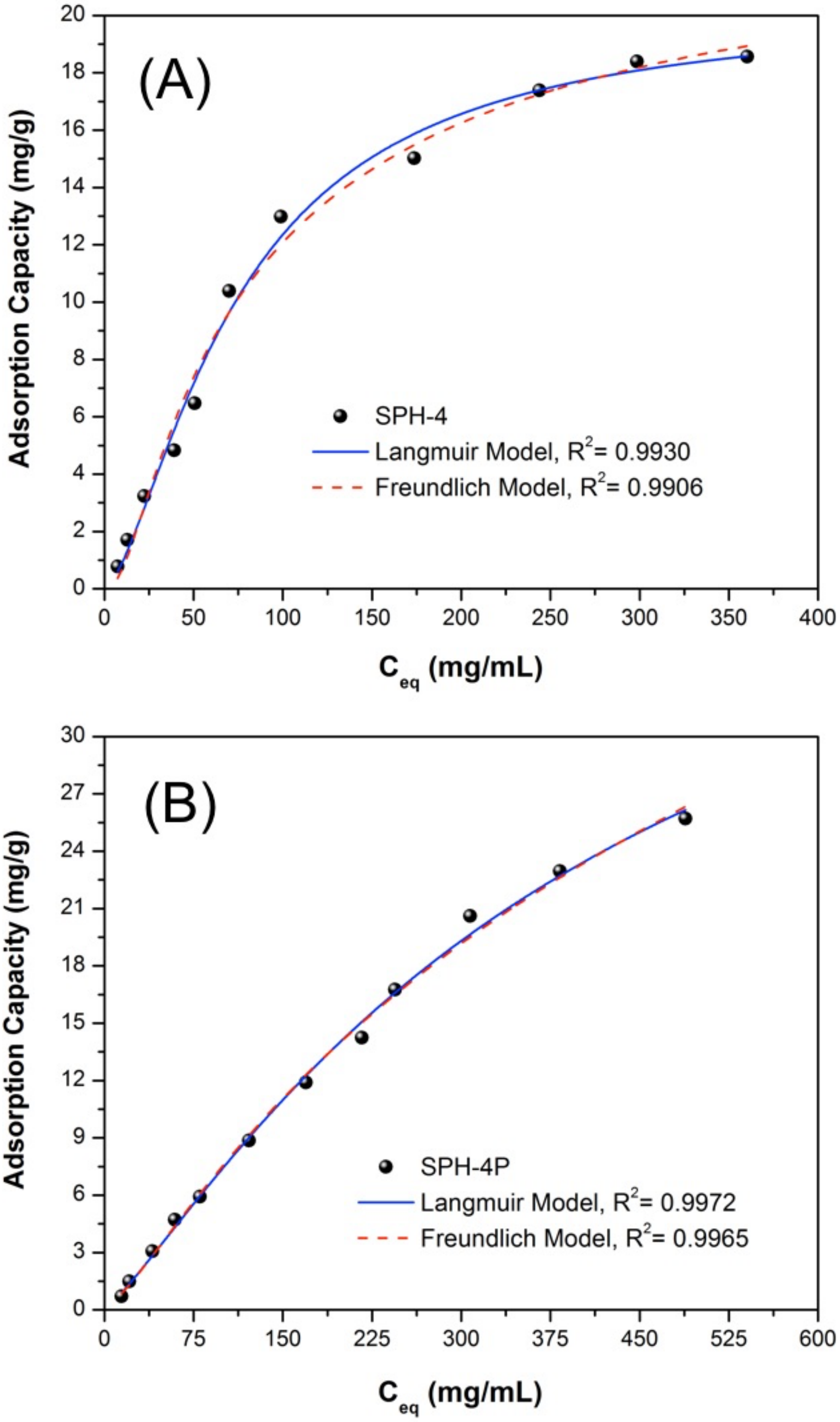


Figure S6. Adsorption isotherm of DEX in SPH-4 (A) and SPH-4P (B). The adsorption isotherms are obtained using the Langmuir (blue solid lines) and the Freundlich (red dashed lines) models.

Table S1. Surface area and pore volume of the SPH aerogels synthesized and studied.

Conditions	**Surface Area (m^2/g)**	**Pore Volume BJH Desorption (cm^3/g)**
SPH-1[a)]	0.04	-
SPH-2[a)]	N/A	-
SPH-3[a)]	0.17	-
SPH-4[a)]	0.20	-
SPH-5[a)]	0.02	-
SPH-6[a)]	0.02	-
SPH-4P[b)]	0.03	-
SBA-15[c)]	252.00	0.42
SBA-15[d)]	303.00	0.59

[a)] These aerogels (SPH-1 to SPH-6) contain mesoporous silica nanoparticles whose internal pores are functionalized with HMDS using toluene as a solvent. [b)] This aerogel contains mesoporous silica nanoparticles whose internal pores are modified with HMDS using 2-propanol as a solvent. [c)] SBA-15 mesoporous silica nanoparticles whose internal pores were modified with HMDS using toluene as a solvent. [d)] SBA-15 mesoporous silica nanoparticles whose internal pores were modified with HMDS using 2-propanol as a solvent.

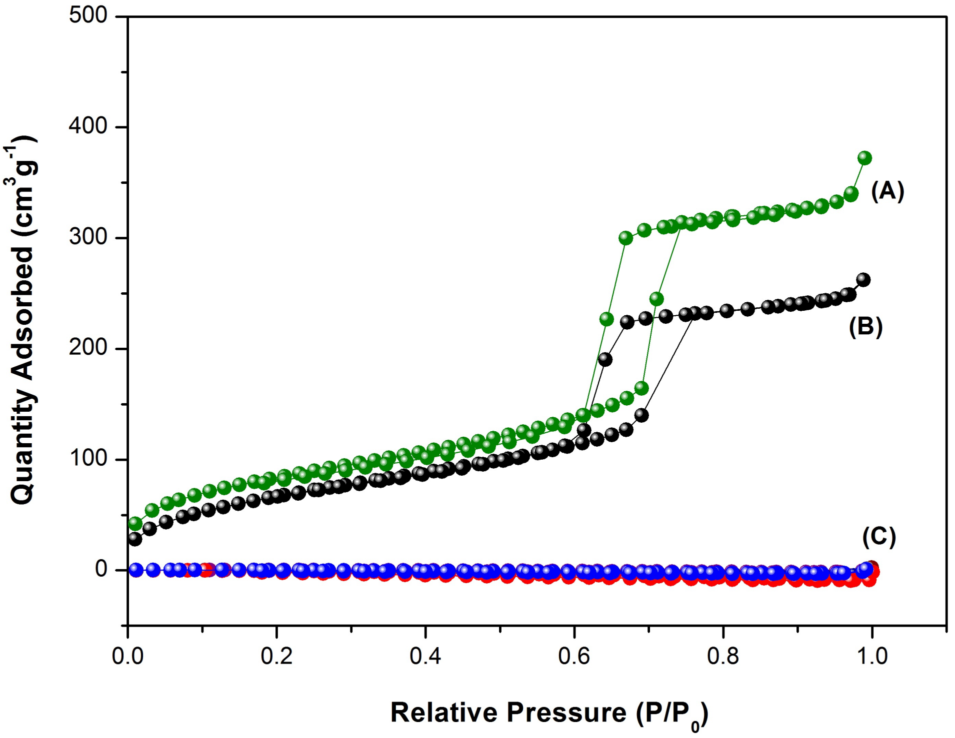


Figure S7. N_2 adsorption/desorption isotherms of SBA-15 mesoporous silica nanoparticles whose internal pores are functionalized with HMDS using 2-propanol as a solvent (A) and using toluene as a solvent (B). (C) N_2 adsorption/desorption isotherms of SPH-1 to SPH-6 aerogels.

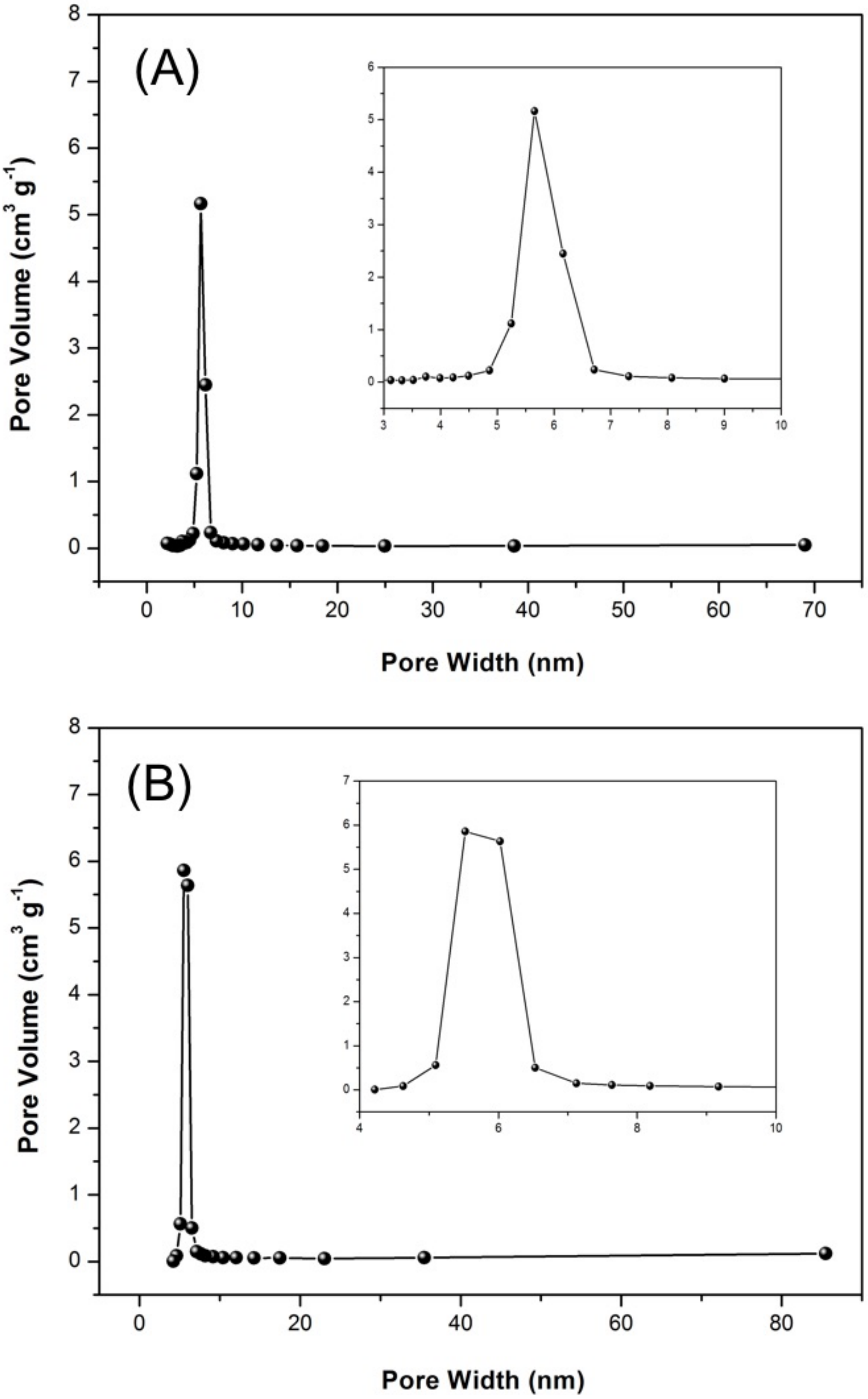


Figure S8. Pore size distributions of SBA-15 mesoporous silica nanoparticles whose internal pores are functionalized with HMDS (A) using toluene as a solvent and (B) using 2-propanol as a solvent.

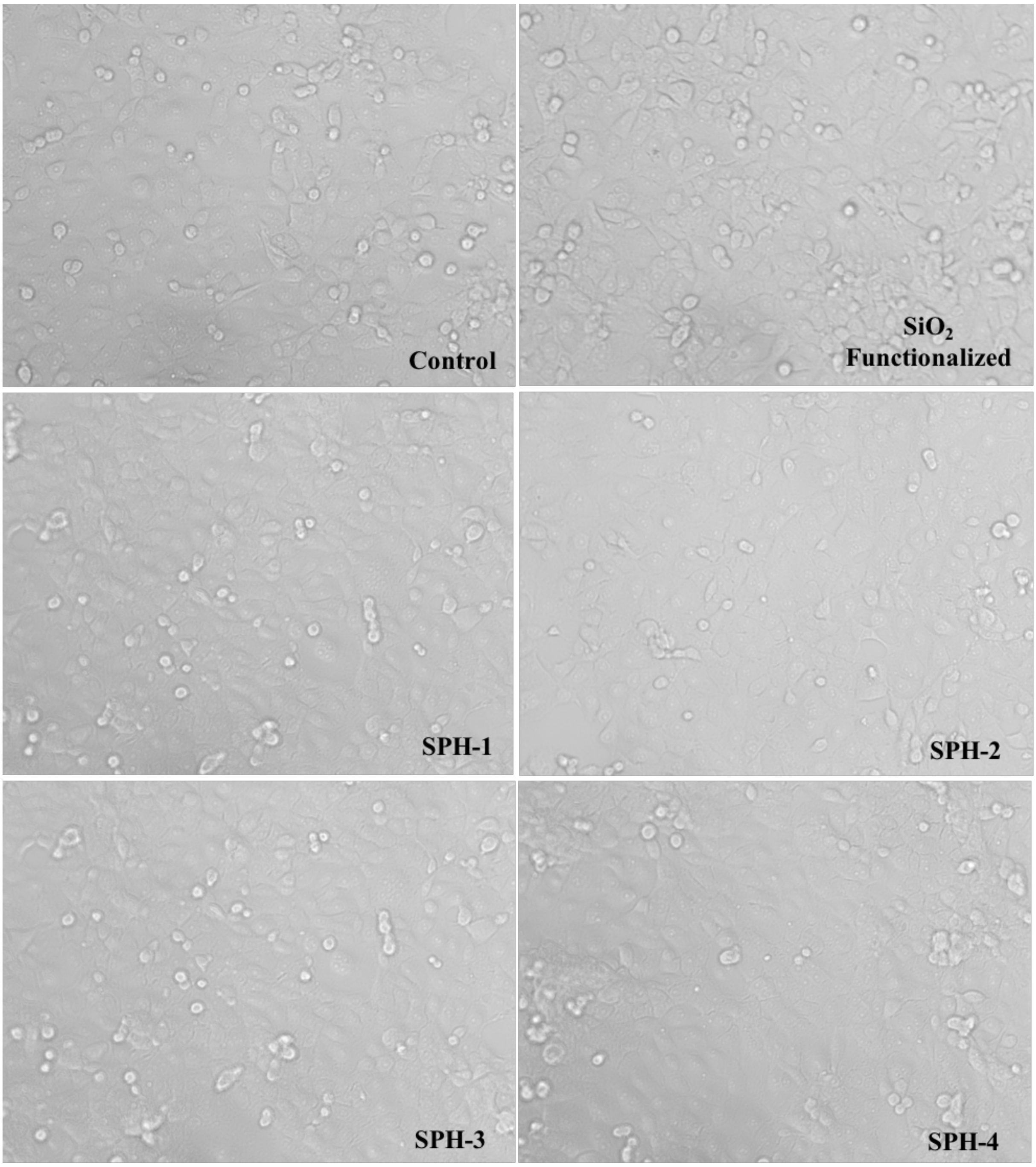


Figure S9. Optical microscopy of Vero cells after 72 h of incubation with different aerogel materials and a control. Magnification: 100-fold increase in blue filter.

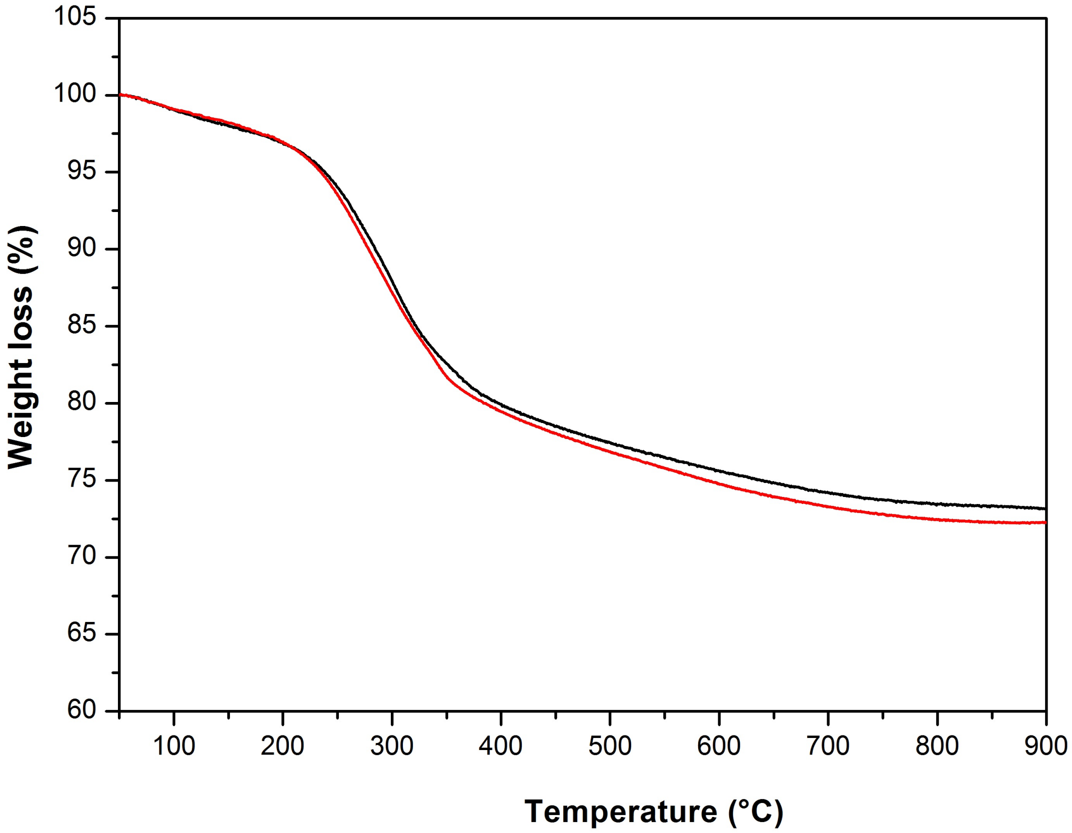


Figure S10. TGA traces of SBA-15 mesoporous silica nanoparticles whose internal pores are functionalized with HMDS using 2-propanol as a solvent (black line) and using toluene as a solvent (red line).

Antibacterial Susceptibility Testing

The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) results of nanoparticles are summarized in Table S2. The *in vitro* results were classified according to the MIC value described by Brambilla *et al.*[1] For values smaller than 100 µg/mL, the antibacterial activity was considered good; for values between 100 and 500 µg/mL the activity was considered moderate; for values between 500 to 1000 µg/mL the activity was considered weak; and for values larger than 1000 µg/mL the nanoparticles did not present activity. Based on the results in Table S2, it can be said that the functionalized silica displayed bactericidal activity against all the strains studied, with better results especially against *S. aureus* (gram positive) and *B. subtilis* (gram positive) compared with *E.*

coli (gram negative) and *P. aeruginosa* (gram negative) bacteria. The pure silica did not show antibacterial activity. These results are expected since the external walls of the functionalized SBA-15 mesoporous silica particles were intentionally functionalized with quaternary ammonium groups, which have bactericidal activity. These groups exhibit bactericide activity due to their permanent positive charges, which interacts strongly with the negative charges on bacterial membranes, causing membrane rupture.[2] The different values found to the gram positive and gram-negative bacteria could be attributed to the outer membrane barrier, existent only in gram-negative bacteria.

Table S2. Minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) of pure silica and functionalized silica.

	MIC (μg/ml)	MCB (μg/ml)	MIC (μg/ml)	MCB (μg/ml)
Strains	Functionalized Silica		Pure Silica	
E. coli	250.0	500.0	>1000.0	N/E*
S. aureus	62.5	125.0	>1000.0	N/E
B. subtilis	125.0	125.0	>1000.0	N/E
P. aeruginosa	250.0	250.0	>1000.0	N/E

* Not evaluated

References

1. L. Z. S. Brambilla, E. H. Endo, D. A. G. Cortez and B. P. Dias Filho, *Revista Brasileira de Farmacognosia*, 2017, **27**, 112-117.
2. H. D. M. Follmann, A. F. Martins, T. M. Nobre, J. D. Bresolin, T. S. P. Cellet, P. Valderrama, D. S. Correa, E. C. Muniz and O. N. Oliveira, *Carbohydrate Polymers*, 2016, **137**, 418-425.