Supplementary Material

HYBRID BIOMATERIAL BASED ON POROUS SILICA NANOPARTICLES AND PLURONIC F127 FOR SUSTAINED RELEASE OF SILDENAFIL: *IN VIVO* STUDY ON PROSTATE CANCER

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A. MATERIALS AND METHODS

A1. MSNs synthesis and characterization

The silica nanoparticles morphology was analyzed by transmission electron microscopy (TEM) in the bright field mode (TEM-BF, Zeiss Libra 120, operating at 80 kV). Nanoparticles surface area, pore volume and pore diameter were obtained through nitrogen-sorption experiments (Accelerated Surface Area and Porosimetry System ASAP 2020 Micromeritics). The Brunauer-Emmett-Teller (BET) method was used to calculate surface area and the Barrett-Joyner-Halenda (BJH) method to calculate the pore diameter, both through the N_2 adsorption branch. The pore volume was calculated from the single-point value adsorbed at P/P_0 = ~0.94.

Zeta potential and hydrodynamic radius measurements through dynamic light scattering (DLS) were carried out using 0.250 mg mL^{-1} of nanoparticle concentration in various dispersant media, and different PF127 concentrations (see Table SM-1). In all zeta potential measurements it was used 10x-diluted PBS solutions. For the measurements, it was used the equipment Malvern ZetaSizer-Nano ZS. MSNs in PF127 solutions were only studied in 0.1-1.0% of PF127 due to the high viscosity of the PF127 solutions above 1.0%.

A2. Colloidal stability assay

To evaluate the effect of PF127 on the MSNs colloidal stability, a centrifugation study was performed. MSNs (1.0 mg mL^{-1}) were incubated with different PF127 concentrations and centrifuged at different relative centrifugal forces (rcf: 90, 2340, 9400 and 18400) for 5 minutes. The amount of silica in the supernatant was quantified by ICP-OES (Inductively Coupled-Plasma Optical Emission Spectrometry, PerkinElmer Optima 8300). In this technique, the sample is atomized or ionized through a high-temperature-plasma that not only dissociates the atoms but also generates a high collision excitation and ionization. By decaying to electronic ground states, the atoms or ions can emit photons in specific wavelengths. Once our sample comprises MSNs with a high stability (against dissolution) in neutral pH, it was necessary to ensure the complete degradation of silica particles into monomeric Si species. Thus, the samples were dissolved in pH 12.0 by adding a 0.01 mol L^{-1} solution of KOH. This pH ensures the silica dissolution into $HSiO^{3-}$ or SiO^{3-},[1] enabling atomization of the sample. To avoid damages to the equipment, samples were neutralized with HCl 0.01 mol L^{-1} prior to each measure, preventing re-precipitation in neutral pH.

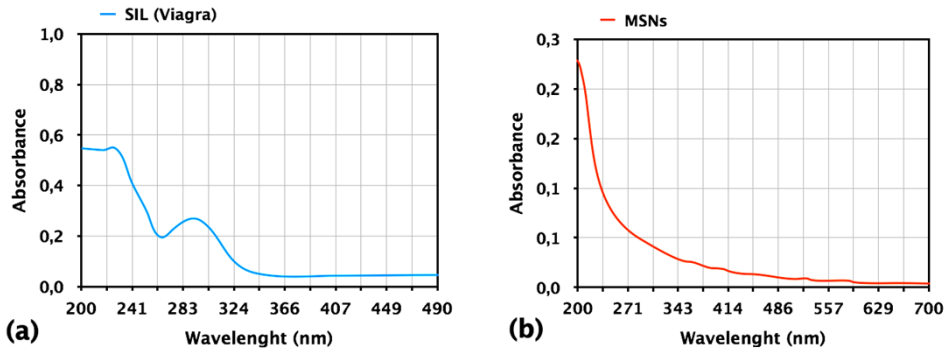

Fig. SM-1. UV-Vis light absorbance spectra of **(a)** SIL (35 µg mL^{-1}) and **(b)** MSNs (250 µg mL^{-1}).

B. RESULTS

B1. MSNs characterization

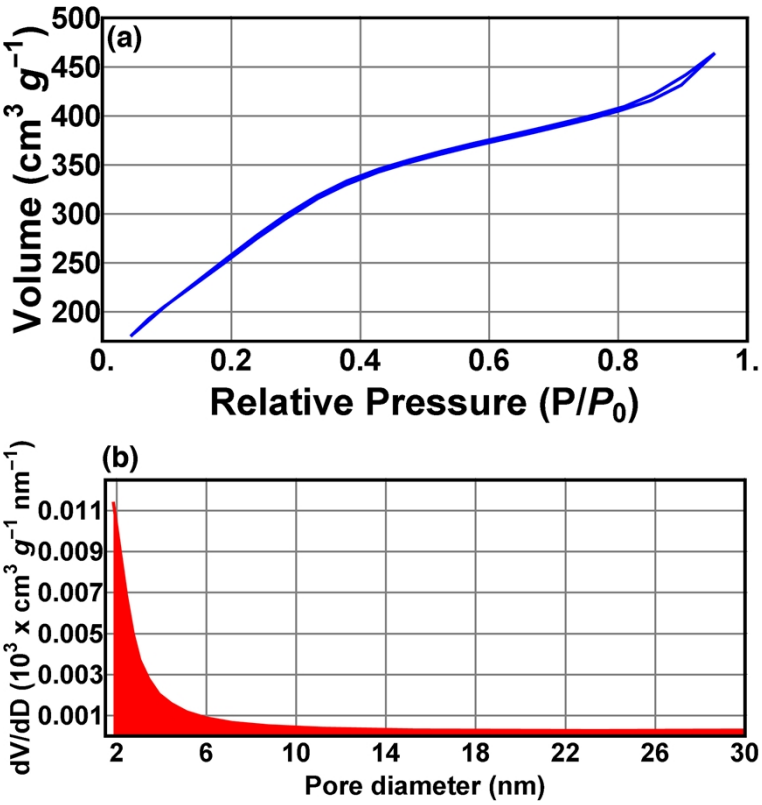

Fig. SM-2. (a) Nitrogen-sorption isotherm of MSNs, **(b)** Pore size distribution indicating pores around 2 nm.

Table SM-1. Characterization of MSNs regarding their size and zeta potential.

	MSNs in dry state	MSNs in water	MSNs in NaCl 0.9%	MSNs in PF127 0.1%	MSNs in PF127 0.5%	MSNs in PF127 1.0%
Size (nm)	45-75*	117.8±4.6	120.7±5.3	150.0±4.3	143.9±6.7	168.8±12.5
PDI	-	0.17±0.05	0.19±0.01	0.18±0.05	0.17±0.01	0.25±0.02
Zeta (mV)	-	−20.0±1.0	−10.8±1.1	−1.5±0.1	−1.5±0.4	−1.3±0.3

* Measured in TEM images.

B2. Colloidal stability assay

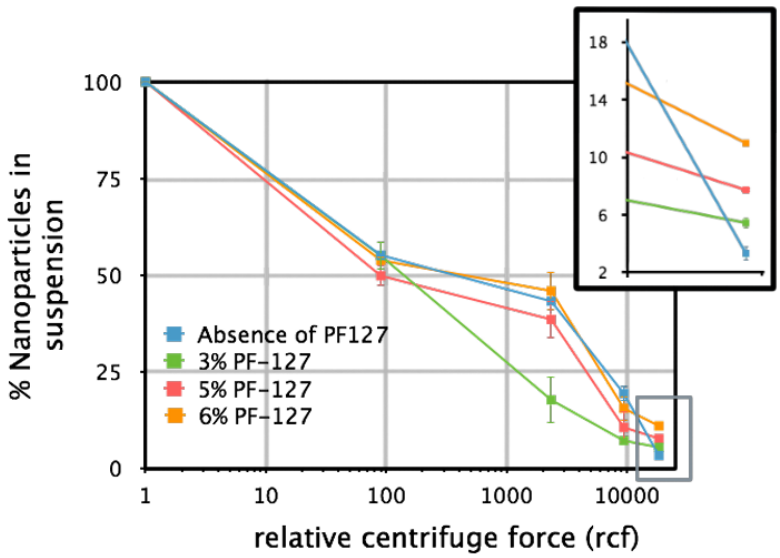

Fig. SM-3. Colloidal stability of MSNs (500 μg mL^{-1}) in NaCl 0.9% (w/v) and in different PF127 concentrations.

REFERENCES

[1] Brinker CJ, Scherer GW. Hydrolysis and condensation II: silicates: In: Brinker CJ, Scherer GW, editors. *Sol-gel Science: the physics and chemistry of sol-gel processing*. San Diego: Academic Press; 1990, p. 97–228.