Stimulus Responsive Breakable Porous Organosilica Nanoparticles

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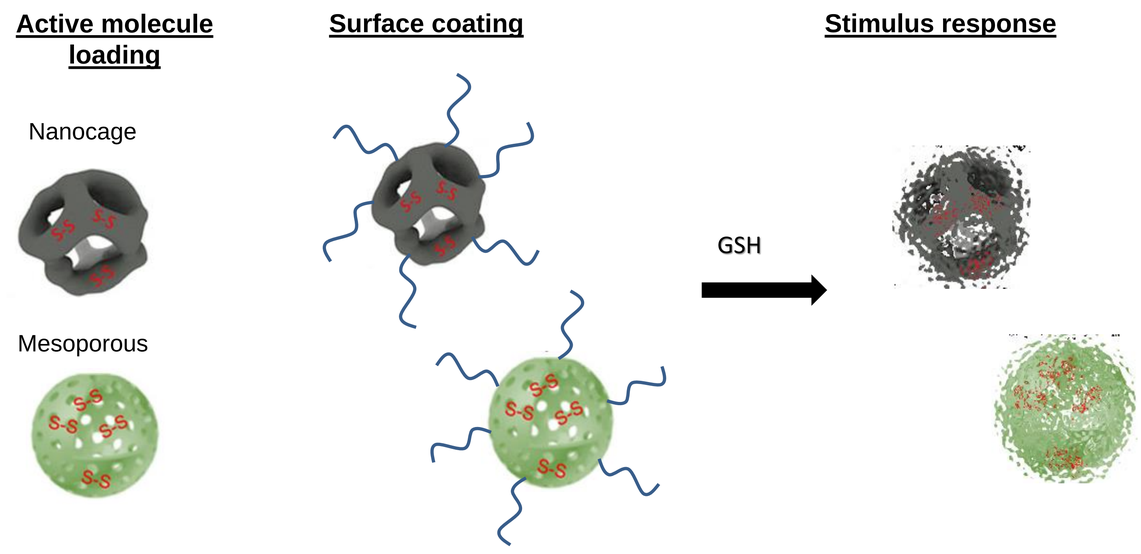
Introduction

Over the last decades, significant progress has been made in the use of nanoparticles for biomedical applications proving their potential for drug-delivery systems [1]. The control of the fate of the nanoparticles once internalized in the cells plays a mayor role to assure not only efficacy but to avoid toxic phenomena [2]. The unique physical and chemical properties of organosilica nanoparticles make them a promising approach for drug accumulation at a target site. An advantageous approach to dope them to respond with self-destructive behavior to stimuli aims into translation in nanomedicine technologies [3]. This work reports the physicochemical investigation and stimulus response of two disulfide-bridged nanoparticles, which can be degraded by glutathione, organosilica nanocages-OSC and mesoporous nanoparticles-MSN.

Self-organized nanoparticles synthesis



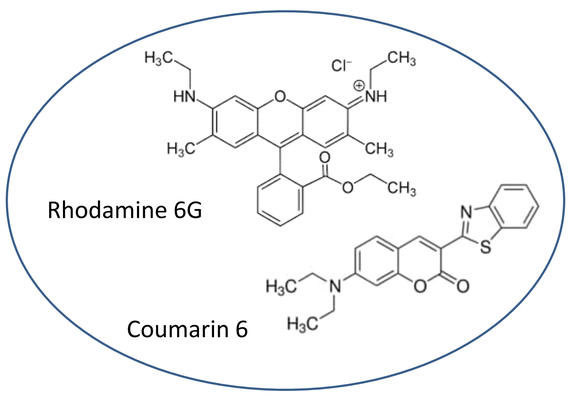
The synthesis is based on a two-step bottom-up procedure in which tetraethyl orthosilicate (TEOS) was hydrolyzed and co-condensed with bis(triethoxysilylpropyl) disulfide (BTDS) in the presence of the surfactant cetylammonium bromide (CTAB) under basic aqueous conditions. Co-condensation of BTDS ensured covalent linkage of the disulfide functional groups within the particle framework, resulting in biodegradable organosilicas. Active molecules (dyes, drugs, etc) can be loaded in their mesoporous core[4].

Increased biocompatibility and steric stabilization were obtained by functionalizing the nanoparticles with polyethylene glycol.

Finally, the purification from unreacted reagents and the surfactant CTAB is done by dialysis of the particles against ethanol/H2O/acetic acid mixture (48 h), ethanol/H2O mixture (24h) and finally against deionized water (24 h) yielding our porous nanoparticles.

Features

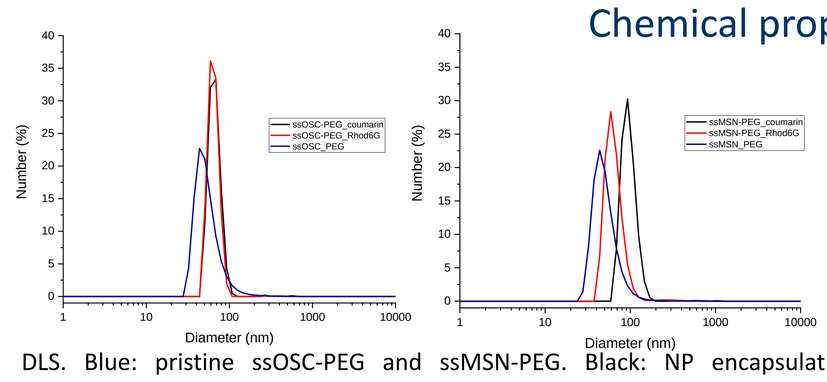
Active payloads



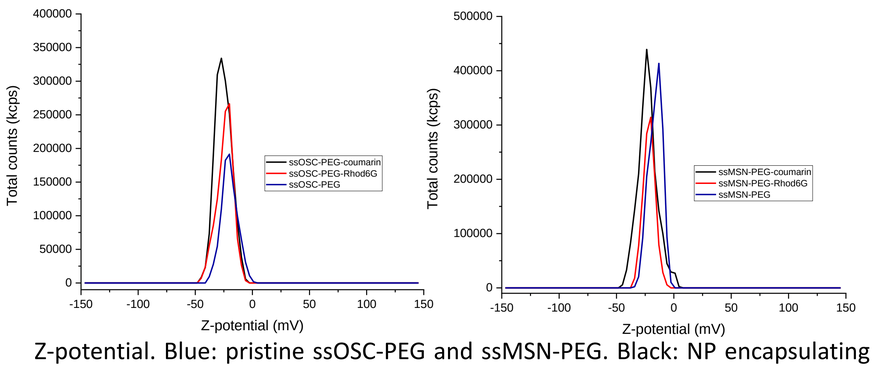
- ✓ Rhodamine 6G hydrophilic and positively charged
- ✓ Coumarin 6 hybrophobic and neutrally charged

- ✓ Hydrodynamic size 60-90 nm
- ✓ Core size (by TEM) 20 nm
- ✓Z-potential before encapsulation -18 mV
- ✓Z-potential after encapsulation -21 mV
- ✓Dye loading 5%
- ✓Surface coverage 15%

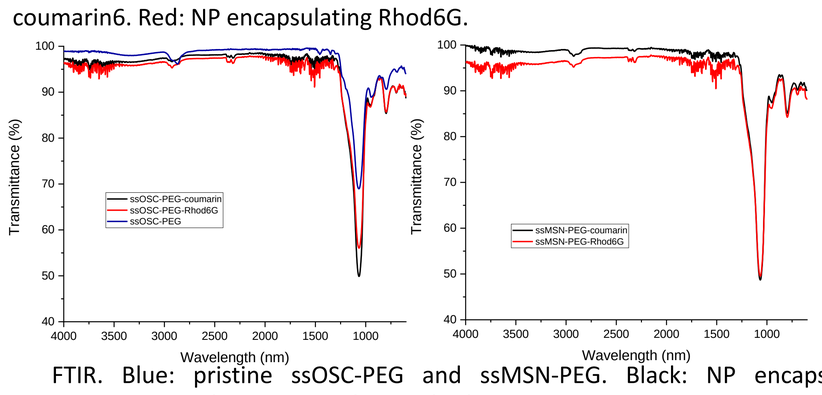
Chemical properties



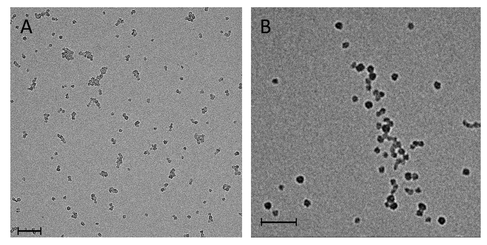
DLS. Blue: pristine ssOSC-PEG and ssMSN-PEG. Black: NP encapsulating coumarin6. Red: NP encapsulating Rhod6G.



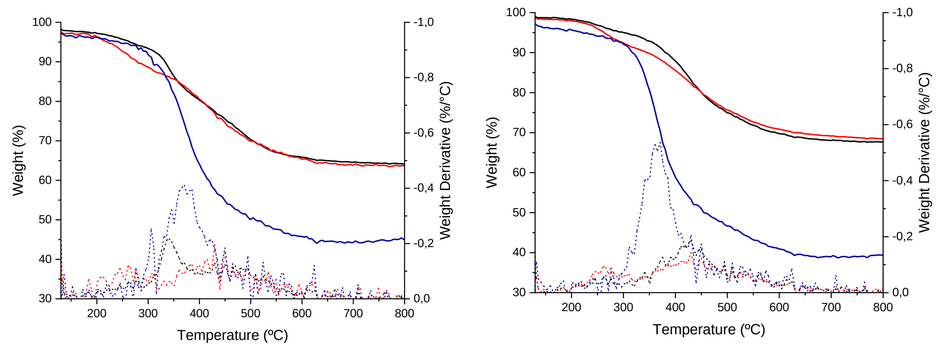
Z-potential. Blue: pristine ssOSC-PEG and ssMSN-PEG. Black: NP encapsulating coumarin6. Red: NP encapsulating Rhod6G.



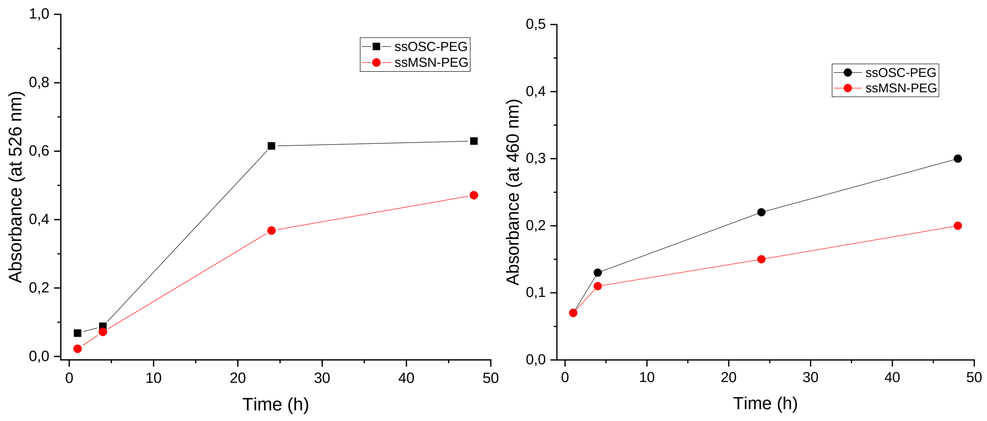
FTIR. Blue: pristine ssOSC-PEG and ssMSN-PEG. Black: NP encapsulating coumarin6. Red: NP encapsulating Rhod6G.



TEM. Scale bar 100nm.
A) ssOSC-PEG. B) ssMSN-PEG



TGA. Left) ssOSC-PEG in blue, NP encapsulating coumarin6 in black and NP encapsulating Rhod6G in red. Right) ssMSN-PEG in blue, , NP encapsulating coumarin6 in black and NP encapsulating Rhod6G in red.



Release of dye incubated with 10 mM GSH in PBS at rt monitored over 48h. Left: Rhodamine 6G. Right: Coumarin 6.

Conclusions

A redox-responsive mesoporous silica nanoparticle was used to encapsulate both hydrophobic and hydrophilic active molecules. Their different morphology, honeycomblike mesoporous nanoparticles and cake-like nanocages showed a different kinetic response to external glutathione stimulus, with the consequent release of active molecules. The nature of the active molecule results in different kinetic release.

Our findings suggest that these nanosystems hold the potential to be used as stimulus responsive nanotools for drug delivery. Further surface functionalization will be studied to specific targeting.

References

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Acknowledgments

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