

## A new one-pot procedure to obtain size-controlled, stealth silica nano-spheres for photodynamic therapy

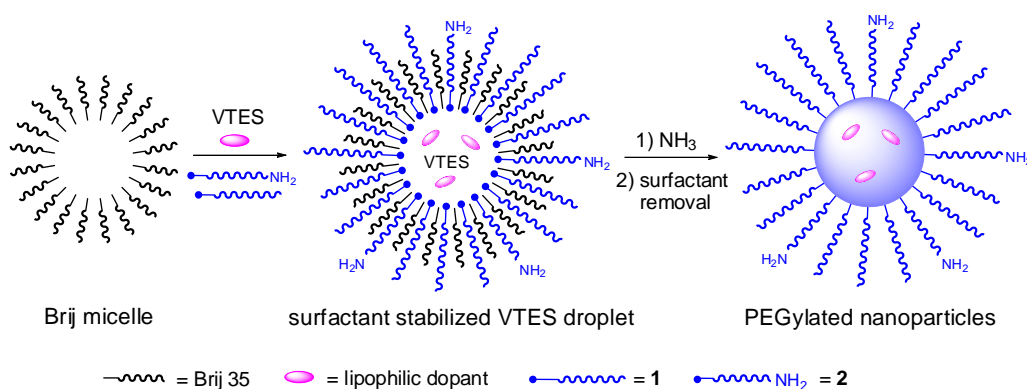
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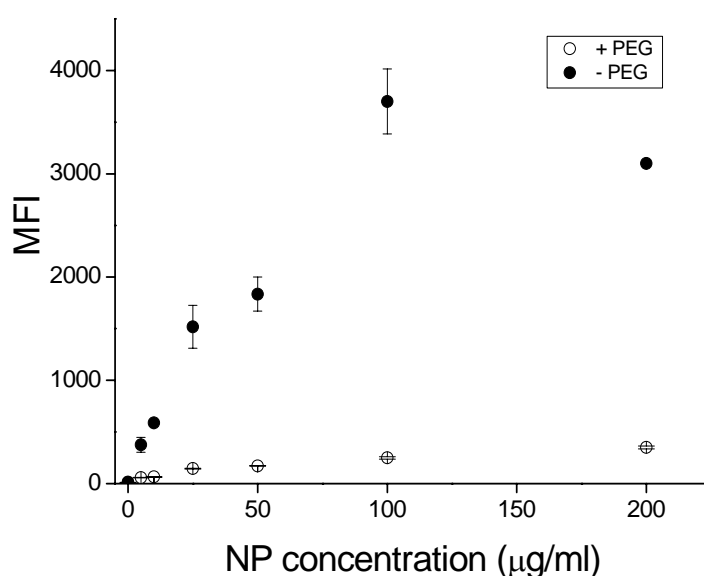
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Silica nanoparticles are cheap, easy to prepare, water soluble, relatively chemically and photo-chemically inert. They can be functionalized (or doped) either at the surface or in the interior. These remarkable qualities make silica nanoparticles excellent candidates as drug carriers and, in general, as nanotherapeutic agents. Nanosized objects are expected to improve the efficacy and selectivity of cancer therapies thanks to passive and active targeting mediated by surface-linked onco-specific ligands. We here report that ammonia-catalyzed polymerization of vinyltriethoxysilane (ORMOSIL ORganically MOdified SILica) in the presence of surfactants, applying a modification of the Prasad method ( I. Roy et al., J. Am. Chem. Soc. 125 (26) (2003) 7860-7865), which is schematized here:



This method allowed the production of NPs with a desired size in the range between 20 and 100 nm by a one-pot procedure. By including a trialkoxysilane modified PEG in the reaction we obtained an unprecedented dense PEG coating of the nanoparticles (30-60% depending on NPs size). Bare or PEG-modified NPs were not toxic to epithelial and blood cells. The ability to evade capture by phagocytic cells (*stealth property*) of our nanoparticles was tested in vitro with human monocyte-differentiated macrophages.

Flow-cytofluorimetry (shown in the figure below) and confocal fluorescence microscopy analysis demonstrated that, while the non-PEGylated silica NPs were efficiently endocytosed in acidic phagosomes, their PEG-coated versions eluded macrophage association and internalisation.



Preliminary data prove that ORMOSIL NPs may be used for the delivery of meta-tetra(hydroxyphenyl)chlorin (mTHPC), a photosensitizers (PS) for photodynamic therapy (PDT), to tumour cells. Since mTHPC entrapped in the NPs was rapidly release in the presence of physiological serum concentrations the characterisation of covalently linked mTHPC to the NP matrix is under investigation.

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