Research and Development

Extended Abstract

Nanomedicine 2017: Inorganic coating of luminescent porous silicon for nanomedicine applications- Nicola Daldosso- *University* of Verona, Italy

Abstract

Porous silicon (pSi) is a photo-luminescent material produced by electrochemical etching of crystalline silicon wafer. It is suitable for nanomedicine applications, because it is inert, biodegradable, bio-compatible and have no immune response. Furthermore, their optical properties, due to quantum confinement effect, are very interesting in perspective of bio-imaging applications. One of the main issues for the exploitation of the pSi micro-particles in nano-medicine is the fast quenching of the optical properties in aqueous environment. We previously demonstrated long-term optical stability by covalent attachment of polymers such as chitosan and PEG. In this work, we studied the optical properties stabilization of the micro-particles in a biological buffer (e.g., PBS) by depositing an inorganic TiO2 layer by ALD (atomic layer deposition) in a rotary reactor. This process allows the deposition of a uniform layer with a fine tuned thickness. By optimizing the ALD parameters, we stabilized the optical properties of pSi micro-particles for more than three months (up to now). We investigated the effect of pSi-TiO2 micro-particles on human dendritic cells (DCs) by in-vitro tests, finding no reduction of the DCs viability, but, in view of nanomedicine applications, their ability to increase the immune cell activation by other agonists has to be considered. These results and their proved photoluminescence stability in aqueous solutions gave the chance to pSi-TiO2 micro-particles to be a promising candidate for nanomedicine applications.

Nanomaterials that will circulate in the body have great potential for the diagnosis and treatment of diseases. For such applications, it is important that nanomaterials are safely eliminated from the body within a reasonable period of time after they perform their diagnostic or therapeutic functions. Despite efforts to increase their targeting efficiency, the mononuclear phagocytic system cleans significant amounts of systemically introduced nanomaterials before finding their targets, which increases the likelihood of unintentional acute or chronic toxicityHowever, there has been little effort to design the self-destruction of wandering nanoparticles in non-toxic and systemically eliminated products. Here, we present luminescent porous silicon nanoparticles (LPSiNPs) that will carry a payload of drugs and whose intrinsic near-infrared photoluminescence allows monitoring both of accumulation and degradation in vivo. Furthermore, in contrast to most optically active nanomaterials (carbon nanotubes, gold nanoparticles and quantum dots), LPSiNPs self-destruct during the mouse model into renal-purified components for a relatively short period of time with no evidence of toxicity. As a preliminary in vivo application, it demonstrates tumor imaging using dextran-coated LPSiNPs (D-LPSiNPs). These results

demonstrate the replacement of a multifunctional low toxicity degradation nanostructure for in vivo applications.

Nanostructured materials have become promising candidates for drug delivery, especially for cancer treatment1. in addition to traditional drug delivery systems based on polymers and lipids (DDS) and other inorganic nanomaterials 2,3,4,5 porous Si (pSi) is a beautiful material for applications in nanomedicine due to its unusual properties, such as a huge area (up to 800 m2 · g - 1) 6, biocompatibility7,8,9 and biodegradability 10,11,12 while maintaining the bioactivity of the drug13. moreover, the nanostructured pSi showed unique optical14 and luminescent properties11,15, which are favorable for the self-declaration of the load and the release of drugs. The pSis are often manufactured in films 6,16,17,18,19,20, microparticles 21,22,23 or nanoparticles 11,24,25,26,27. The loading capacities of the drugs and the release kinetics depend strongly on the area and the surface chemistry of the materials pSi28,29. And not surprisingly, hydrophobic preparations are more efficiently loaded into hydrophobic pores 17.28. However, often when used under physiological conditions, drug reservoirs are often difficult to moisten with hydrophobic exterior surfaces. Thus, pSi decorations on the inner and outer surfaces with various properties are very popular.

A selective modification on the external surfaces of pSi was reported for the first time by Cunin and his colleagues31. Here, the flat silicon was thermosilylated thermally with hydrocarbons, followed by an electrochemical etching. The organic layer remained at least partially on the outer surface while fresh pores were presented, leaving the inner surfaces available for further modification. For inner surface modification, several anodization and silanization cycles were applied on alumina membranes, leading to spatially controlled surface modifications32,33. Kilian et al. presented a differential functionalization on exterior and interior pSi surfaces which relied on the mixture of physical phenomenon and capillarity30, the entire surface was first modified with hydrophobic 10-succinimidylundecenoate which could effectively repel water from penetrating the internal pores, leading to peptide conjugation occurring only on the external surfaces. On the other hand, using organic solvents, various reagents were attached to the internal surfaces of pSi. In the same way, Wu and Sailor used an inert fluid as a "mask" to protect the internal pores from exposure to the acid solution during the selective functionalization of the external surface of pSi34. A three-step functionalization procedure has recently been described, consisting of two hydrosilylation reactions separated by selective digestion of the outer surface. This procedure provides the outer surface of pSi with hydrophilic groups, limiting hydrophobization to the inner pore walls, as demonstrated by angular resolution X-ray spectroscopy (XPS) using pSi35 macropores. A less dependent pore size procedure was also reported in which the hydrosilylation reaction using light resulted in discrete surface chemistry of the pSi layers, where the depth of the chemical modification depends on the wavelength of sunlight used in the procedure36. However, pSi exterior surface modification with polymers, especially anti-fouling polymers, while decorating interior pore walls with hydrophobic species has not been demonstrated thus far.

The Si platelets were purchased from Siltronix in France. All chemicals (reagents and solvents) used for the synthesis were purchased from Sigma-Aldrich with the best available purity and used as indicated,

unless otherwise specified. For the Europium test, reagents such as DELFIA boosting solution and 100 nM European standard were obtained from PerkinElmer, Australia. Human albumin (HSA, 99%) and fibronectin (FN) were purchased from Sigma-Aldrich. The following reagents were used for cell culture: paraformaldehyde (Sigma), DMEM medium (Invitrogen), fetal bovine serum (FBS, Invitrogen), Triton ™ X-100 (Sigma) and 4 ', 6-diamidino-2-phenylindole (DAPI) (Invitrogen) and all were used as received. Mouse L929 fibroblast cells were used in cell culture experiments. N- (2-hydroxypropyl) acrylamide (HPAm) and N-benzophenone acrylamide (BPAm) were synthesized as previously reported.

Inorganic structures such as smart nano transporters for drug delivery combine recent research on inorganic drug delivery structures. various types of nanocarriers are presented and discussed in detail, providing a modern overview of inorganic nanoparticles with pharmaceutical applications. This book has been written by various international scientists and may be a valuable reference for researchers in the biomaterials, pharmaceuticals, and people who want to learn more about the current applications of inorganic intelligent nanocarriers.

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