NANOENGINEERED HYBRID SILICA/ORGANIC NANOPARTICLES AND IONIZED GASES FOR BONE REGENERATION THROUGH SMART SCAFFOLDS

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Introduction

The use of degradable scaffolds promoting stem cells adhesion and proliferation is one of the most promising approaches today in tissue regeneration. However, this approach is still facing many challenges such as cost, mechanical properties and shaping of the scaffolds, revascularization of tissues, drug delivery on long durations and the ability of the scaffolds to promote efficiently the cells adhesion and proliferation. A way to solve a part of these challenges is to embed or attach specifically engineered nanoparticles into these scaffolds and to treat these scaffolds by ionized gases. Silica-based mesoporous nanoparticles are particularly well suited for the bone regeneration due to their slower dissolution rate in physiological media, their high drug loading capacity, their high ability to be functionalized by biodegradable coatings and their biocompatibility. In this work, two approaches are studied to improve the scaffold properties for bone regeneration through mesoporous silica nanoparticles and ionized gas. The first one is based on silica nanoparticles functionalized with biocompatible coatings made of lipids or/and polysaccharides. By this way, active molecules are well protected during their attachment to the scaffolds or during sterilization processes. And active molecules release can be better controlled. In the second approach, ionized gas is used to allow the functionalization of the scaffolds for nanoparticles attachment, sterilization and promotion of cell attachment and proliferation. The interaction of silica nanoparticles and ionized gas with scaffolds will be discussed. As a first result, a good dispersion of these nanoparticles has been obtained in polymeric scaffolds as monitored with the fluorescent probes placed inside the nanoparticles.

Materials and Methods

Mesoporous silica nanoparticles with a pore size around 10 nm were synthesized using a sol-gel approach in alkaline conditions [1]. A surfactant, CTAB, a swelling agent and a base, TEA, are added in a hydro alcoholic solution at room temperature and stirred. Then, the temperature is increased to 60°C and the silica precursor, TEOS, is added drop-by-drop in this mixture. The solution is stirred during 2h at 60°C. APTES is added 20' after TEOS in order to get amine chemical groups on the external part of the silica nanoparticles. These inorganic nanoparticles are then coated with a lipid bilayer and a calcium alginate coating by using cycles of mixing, ultrasonication and centrifugation [2], or with a polysaccharide multilayer by using the layer-by-layer approach [3]. Finally, these hybrid nanocarriers are embedded in a polymer scaffold made of polycaprolactone containing polyurethane units [4]. For plasma activation of the scaffold, a pulsed radio-frequency plasma jet Neoplas KinPen 11 working at atmospheric pressure was applied either directly on the scaffold in air or with a film of water on top [5].

Results and Discussion

The pore size was controlled by adding a swelling agent, ethyl acetate, in the hydroalcoholic solution with the other reactants. The ethyl acetate molecules are swelling the micelles formed with the surfactant, up to 10-15 nm, leading to pores of similar size after cleaning/dissolution processes, without changing the main characteristics of the nanocarriers synthesized without swelling agent, including the particles diameter (50-80 nm) as shown on FIG. 1. By this way, proteins can be encapsulated and protected, after adding an organic coating, inside these nanocarriers before to be embedded in the scaffold.

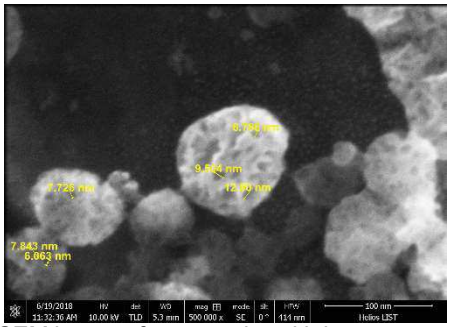

FIG. 1. SEM image of nanocarrier with large pores.

The different organic coatings deposited on the silica core nanoparticles were shown to avoid active molecule leakage and provide a good biocompatibility to the hybrid nanocarriers. Then, two approaches are targeted to attach the nanocarriers to the polymeric scaffold. In the first one, the scaffold has to be activated by the ionized gas jet in order to generate chemical groups able to react with the organic coating of the nanocarriers. It is shown that both in water and air, O-containing groups are formed in a range of 1% in water to few percent in air by applying the plasma jet for a few minutes on the scaffold. These functional groups will allow to attach the hybrid nanocarriers more easily to the scaffolds. In the second approach, the hybrid nanocarriers are directly suspended in the emulsion used to generate the porous scaffold. By this way, a homogenous dispersion of the hybrid nanocarriers was obtained.

Conclusions

Mesoporous-based silica nanoparticles were synthesized and functionalized in order to be able to protect and deliver proteins for bone regeneration through a polymeric scaffold. Ionized gas was used to prepare scaffolds for attachment of the hybrid nanocarriers. The organic coatings allowed to protect the payload and to disperse the nanoparticles inside the scaffolds. Next steps will focus on up-scaling of nanocarriers and biological tests.

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