POLYMER BASED SCAFFOLDS FOR TISSUE REGENERATION

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To attain a successful ECM analogue scaffold, there are several design and material criteria that must be satisfied involving the mimicking of topographical features and geometry on the macro-, micro- and even at nanoscale levels, because each influences cell response to the scaffold.

In the last years, a successful approach has been represented by the use of composite scaffolds obtained by a combination of phase inversion, salt leaching, filament winding technology. These techniques enable obtaining porous scaffold with controlled micro and macro porosity able to influence positively mechanical properties and cell interactions. In particular, composite materials based on biodegradable polymers (i.e. poly-ε-caprolactone) endowed with intrinsically bioactive particles (i.e. calcium phosphates) and/or macromolecules (i.e Hyaluronic Acid), offers the possibility to realize a strong bond with natural tissues through more bioactive, structurally and mechanically efficient interfaces, firstly enhancing the capability of the substrate to form new extracellular matrix (ECM) and assuring a more rapid and efficacious integration to the implant site. However, some limitations of traditional process impose to identify innovative strategies for fabricating micro and nanostructures structures.

In this context, interesting approaches based on the assembly of basic components or building blocks endowed with molecular signals are powerfully emerging to form hierarchically complex structures, able to accurately recapitulate the functional properties of natural complex structures. For connective tissue regeneration (bone, ligaments, meniscus) composite scaffolds are obtained by phase inversion, salt leaching and RP technique to modulate mechanical properties and cell interactions.

Design of bioactive scaffolds for bone regeneration with appropriate porosity and high pores interconnectivity could be obtained by using Poly(ε-caprolactone) reinforced with Calcium Phosphates particles and PLA fibres.

Ester of Hyaluronic Acid reinforced with degradable fibres were processed by composite technology, phase inversion and salt leaching technique to obtain scaffolds for meniscus regeneration. In vivo results demonstrated the possibility to regenerate the meniscus by using an appropriate scaffolds. Imaging and rapid prototyping technologies are implemented to design a "custom made" meniscus scaffold. A critical discussion on the advantages of new approaches has been performed by proposing strategies based on composite to the assembly of elementary components such as fibres implemented through modified electrospinning or sintering techniques.

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TYROSINE-DERIVED NANOSPHERE FORMULATIONS FOR ENHANCED SKIN DELIVERY

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Purpose

To investigate the skin delivery profiles of polymeric tyrosine-derived nanospheres formulated as aqueous suspensions and hydrogels.

Introduction and background

Tyrosine-derived nanospheres (NSPs) are formed by the selfassembly of ABA-type amphiphilic triblock copolymers derived exclusively from natural metabolites.

The A-blocks are poly(ethylene glycol), PEG, and the hydrophobic B-blocks are oligomers of desaminotyrosyl-tyrosine alkyl esters (DTR) and non-toxic diacids (FIG.1)[1,2]. . These NSPs are biocompatible and previous studies have established their lack of toxicity in KB cervical carcinoma cells and after injection in mice[.1] The versatility of the polymeric architecture of these NSPs (hydrodynamic diameter of about 70 nm) enables effective binding and delivery of a vast array of ipophilic agents[2]. In these studies we evaluated the potential of NSPs as delivery vehicles for highly lipophilic molecules for passive skin permeation. The efficiency of the nanosphere approach was compared to a non-particulate formulation represented by propylene glycol (PG). Nanospheres loaded with the fluorescent dye Nile Red (NR), which has been previously used for visualizing of micelle and liposome distribution within the skin were used in passive permeation studies. The depth and amount of skin penetration of NR after topical application was evaluated in in vitro and in vivo models. We also formulated the NSPs as hydrogels, and compared their in vitro and in vivo skin delivery profiles to the aqueous NSP formulations. Lastly, we evaluated the potential synergistic effect and formulation characteristics of combinations of NSP-hydrogels with the skin penetration enhancer Azone.

Methods

The triblock copolymers were synthesized in a one-pot reaction at 20°C using in situ carbodiimide coupling of the PEG and oligo(DTR-XA). The self-assembly of the nanospheres was induced by drop-wise addition of a solution of the copolymer and the lipophilic dye Nile Red (NR) in DMF into phosphate buffered saline (PBS, pH 7.4) with mild agita-