Executive Summary

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Project "Nanofibres for intelligent drug delivery"

The electrospinning technique is an efficient and versatile technology to produce nanostructured fibres with diameters ranging from a few nano-meters to several micro-meters. The unique characteristics of nanofiber structures such as their high surface-to-volume ratio, tuneable porosity, and/or their structural analogy to the extracellular matrix (ECM) make them suitable architectures for various applications such as tissue engineering, wound healing, controlled release systems, filtration elements (e.g., filtration membranes) and/or high performance functional laminates. In this context, the aim of this research project was to develop biopolymeric electrospun fibres incorporating pharmaceutical active agents (e.g., bone morphogenic proteins Bmp-2) and to use them as drug loaded fibre-scaffolds for tissue engineering and bone regeneration studies. Indeed, in the course of this project, we have demonstrated that drug loaded fibre-scaffolds derived from electrostatic spinning processes offer the possibility to tune their mesh properties with respect to fibre diameter, porosity and surface composition, which can lead to sustained release systems. In this regard, we have designed a novel approach where hierarchically structured fibres architectures incorporating different types of porosities can achieve adjustable release rates. We proved that by using rationalized environmental spinning parameters (e.g., controlled relative humidity) and tailored spinning solvent compositions (e.g., use of non-solvents), fibre formation processes can be directed towards the formation of tailored-made porous architectures. We believe that the drying process of the electro-hydrodynamically formed polymer jet is undergoing selected stages of phase transitions − with regard to polymer solubility and miscibility differences − that leads to the resulting and rationalized tailored-made porous architectures.

In one hand, a first approach involved the utilization of the emulsion electrospinning method in which the pore formation was found to be highly dependent on the environmental humidity conditions and the concentration of the surfactant used for the stabilization of the dispersed phase. For instance, when polystyrene was used at high humidity values and low surfactant concentrations, porous sheaths were obtained with mean pore area values of 6.0 * 10-4 μm2 and 1.0 * 10-3 μm2. However, at low humidity values dense fibre formation was observed. Thereby, water from the atmosphere acts as a non-solvent influencing the drying process during fibre formation, which enables a rationalized structuration of the fibre surface. Release kinetic studies measured for an encapsulated dye molecule (i.e., fluorescein sodium salt) revealed higher release rates for porous fibres, proving the dependencies of fibre structure and release rates.

In a second approach, fibre pore formation was investigated employing different solvent compositions where mixtures of polymer soluble and insoluble solvents for the biopolymers under investigation were used (e.g., poly-ε-caprolactone). It was found, that based on the solubility characteristics of the polymer soluble and insoluble solvent composition, the vapour pressure of the non-solvent and the environmental humidity conditions employed during the electrospinning process lead to the formation of bicomponent fibre structures exhibiting a dense fibre core and a highly porous sheath. Typical dimensions of the core diameters are in the range of 1.5 – 2.0 μm, whereas the sheath revealed thicknesses of 500 nm.

Currently, a systematic study of the influence of the morphological and chemical characteristics of the described nanofibrous architectures on cell growth and their

differentiation is under investigation in our group; we aim at designing new future intelligent substrates for application in the tissue engineering field. As potential candidates, human pre-osteoblasts and/or mesenchymal stem cells are selected as good cell-type scenarios to study their interaction with this newly developed drug release fibre architectures, in terms of the osteogenic differentiation and subsequent proliferation.

Finally, from a technological and industrial point of view, the up-scalability of the electrospinning methods developed within the project was investigated. Parameters such as fibre spinning throughput at constant fibre morphologies and membrane stabilities were investigated using a needleless electrospinning approach. By adjusting viscosities and the electrical conductivity of the spinning solvent, membrane weights of up to 30 g/m2 incorporating thicknesses in the range of 50 µm were obtained; a result that satisfies our expectations.

As a main challenge of this research work, we will outline the stabilisation of the emulsions with respect to the properties of the dispersed phase and the following spinnability and homogeneity of the resulting fibres. It was problematic to obtain emulsions with a stable dispersed phase and with a homogenous desired droplet size. In this regards, different studies considering complex emulsion compositions had to be studied before adequate results were accomplished.