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BIODEGRADABLE ELECTROSPUN VASCULAR GRAFTS AND THEIR TRANSFORMATION IN SITU INTO NEO-ARTERIES (Invited)

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ELECTROSPUN NANOFIBERS FOR ADVANCED WOUND CARE (Invited)

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The global market for advanced wound care is estimated to grow from US\$ 10bn in 2017 to more than US\$ 13bn by 2022. This rapid growth is driven by factors such as the global increase in the incidence of surgical wounds and various ulcer types (diabetic foot ulcers, pressure ulcers, and venous leg ulcers), the aging population, rising R&D activities in this field, and increasing awareness of the improvements in therapeutic outcomes and quality of life offered to patients by advanced wound care therapies.

While the technical and commercial barriers to entry in the market of advanced wound care are high, electrospun fibers present a new category of materials that offer value addition that can be leveraged with existing products and can also be used to create new-to-the-world products. This potential has not fully been realized and there is huge capacity for electrospun fiber-based materials to be applied in developing dressings and devices aimed at controlling infection, managing wound moisture, and reducing scarring.

This talk describes electrospun fiber developments and applications in advanced wound care and looks at commercialization aspects of electrospun fiber products. Some of the aspects covered will include:

- Smart formulations and architectures that directly address the indication at the biointerface;
- The use of a suitable high-throughput electrospinning platform technology;
- The necessity for a good understanding of the regulatory path, economic and reimbursement factors; and
- Clear understanding of the user needs from the design phase.

All of these factors will affect the likelihood of successful transition of novel electrospun fiber based wound care product concepts from the lab to commercial production.

STRUCTURE DEPENDENT CELL ACTIVITY ON PCL/GELATIN AND PCL/COLLAGEN NANOFIBERS ELECTROSPUN FROM VARIOUS SOLVENTS

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Bicomponent nanofibers consisting of polycaprolactone (PCL) and one of the biopolymers, gelatin or collagen, were formed by electrospinning using two types of solvents - hexafluoroisopropanol (HFIP) and the acetic acid (AA) and formic acid (FA) mixture. The electrospinning was optimized previously [1], providing similar morphology for both types of solvents. Cellular *in vitro* tests were performed using L929 mouse fibroblast cells and human primary fibroblasts. MTT cytotoxicity tests performed on extracts, revealed no cytotoxicity irrespective of the solvent used. The results of investigations of cellular activity in direct contact using various methods - SEM, fluorescent dyeing of nuclei and cytoskeleton, DNA proliferation test, and MTT, indicate that the biopolymer addition increases cell adhesion and spreading on the surface of nonwovens. Slightly higher cell

activity observed for nanofibers containing collagen compared to those with gelatin can be explained by non-complete denaturation of the collagen native structure as observed by FTIR. The most important result is that the cellular activity on nanofibers electrospun from HFIP is higher than for nanofibers electrospun from AA/FA. We see two reasons of this observation. The first one is related to different molecular conformation of biopolymers in both type of solvents, as deduced from our viscosity measurements. In the case of strong solvent like HFIP, the molecular conformation is more expanded compared to compact conformation caused by prevailing polymer-polymer internal interactions in weak solvent (AA/FA). The conformation of polypeptide molecules seems to be crucial for accessibility of RGD sequence, with easier access for integrin receptors in the case of more extended conformation in HFIP. The second reason can be attributed to slower leaching of biopolymer from nanofibers electrospun from HFIP compared to the case of using AA/FA, as observed from analysis of biodegradation in PBS solution at 37°C. The origin of differences in the kinetics of biopolymer leaching during biodegradation is related to the structure of solution and hence final nanofibers. In the case of strong HFIP solvent, there is molecular dispersion of polymers, while segregation of components was observed for nanofibers electrospun from weak AA/FA solvent, leading to easier biopolymer leaching.

Acknowledgements

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References

[1] P. Denis, J. Dulnik, P. Sajkiewicz, *Int. J. Polym. Mater.* 64, 354-364 (2015).

CHARACTERIZATION AND EVALUATION OF TPU-HYALURONIC ACID MEMBRANES FOR TISSUE ENGINEERING APPLICATIONS

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The objective of the presented study was the development of an electrospun membrane produced from hyaluronic acid (HA) and thermoplastic polyurethane (TPU). In the fabrication process of the two components TPU/HA-membrane TPU was electrospun from a chloroform/methanol solution while HA was electroblown from an aqueous solution. The resulting membranes feature a broad field of application in the tissue engineering area ranging from the design of artificial heart valve leaflets to skin regeneration.

Stable production parameters for the electrospinning of TPU and the electroblowing of HA were determined in the present study. The correlation between the process parameters and the fibre properties were statistically analysed for TPU. It was found that the fibre diameter increased with increasing polymer concentration and also with increasing relative humidity in the spinning chamber. In order to determine the process parameters for HA a solution parameter assessment was completed to evaluate the fabrication of hyaluronic acid nanoparticles with the electro-blowing technique. The resulting spinning parameters were set to 8 wt% TPU in chloroform/methanol, 1 wt% HA in water, -15 kV on the collector and 20 kV on the spinnerets.

Different test methods were used to characterize the membranes with regard to their usage as artificial scaffolds for different tissue engineering applications. Fourier transform infrared spectroscopy (FTIR) was used to confirm the existence of the two components in one membrane. Scanning electron microscopy (SEM) showed that HA was dispersed as nanospheres and small films inside the TPU fibre matrix. The diameter of the TPU-fibres was also determined from the SEM pictures ($2.1 \pm 0.2 \mu\text{m}$). The mechanical properties were determined in uniaxial stress-strain tests, the measurements showed an ultimate tensile strength of $2.2 \pm 0.4 \text{ MPa}$ and a strain of $110.2 \pm 25.9\%$. Contact angle measurements displayed an enhancement of the hydrophilicity. The contact angle decreased from $108^\circ \pm 0.8^\circ$ for pure TPU-membranes to $83^\circ \pm 1^\circ$ for TPU/HA-membranes. Also the enhancement of the biocompatibility was indicated in XTT-Assays. This study successfully demonstrated the reproducible production of TPU/HA membranes with tuneable microstructures.