Towards heart tissue regeneration: a piezoelectric patch with smart nanocarriers for on-demand drug release

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45% of death in Europe are ascribed to cardiac diseases and myocardial infarction (MI) weighs a large part of them. After an MI, a portion of the myocardium tissue is lost, substituted by fibrous tissue with minimal physiological functions: this can lead to severe heart dysfunction. Available therapies cannot successfully address the problem, therefore there is an urgent clinical need for new solutions. The Horizon Europe REBORN project (https://www.rebornproject.eu/project/) tackles this issue by designing a piezoelectric patch that can stimulate the restoration of healthy tissue by the piezoelectric fibre nanoarchitecture and on-demand drug release by nanocarriers (**Fig. 1**). The modulation of drug delivery can be triggered with different stimuli: within the REBORN project, ultrasounds will be used to control *in-situ* release. Among the various biofabrication techniques, electrospinning (ESP) is the most suitable to produce matrices with properties matching the ones of the cardiac extracellular matrix: aligned nanofibers with high interconnected porosity [1]. Furthermore, ESP provides high flexibility in terms of polymeric formulation that can be used, and it allows the incorporation of drug nanocarriers inside the fibres. The present work aims to exploit ESP with a rotating drum collector for the fabrication of polyvinylidene fluoride (PVDF) piezoelectric polymeric matrices with aligned fibres and the preliminary incorporation of mesoporous silica nanoparticles (MSN) as drug carriers.

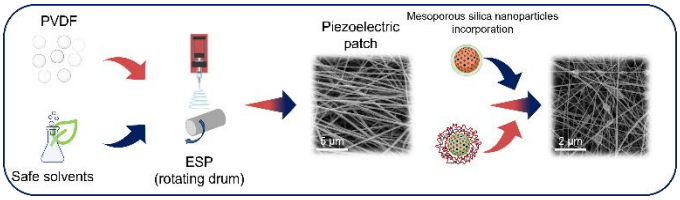

Figure 1 Scheme of the Reborn patch concept

PVDF is a renowned piezoelectric biocompatible polymer largely used for electrospun devices for medical applications [2], and it was chosen to achieve electromechanical coupling with the myocardium. At first, non-toxic solvents to obtain PVDF spinnable solutions, acetone (ACE) and dimethyl sulfoxide (DMSO), were selected from the literature, to avoid possible cytotoxicity of the patch [3]. The effects of different formulations (PVDF concentration, ACE/DMSO ratio) and the ESP process parameters (voltage, flow rate, distance, drum speed) were investigated. The obtained membranes have been thoroughly characterized in terms of morphology, alignment, crystallinity, crystalline phases, mechanical properties, and wettability. By tuning the parameters, it was possible to obtain well-defined fibres, with a diameter of around 300 nm, and a good alignment. The piezoelectricity of PVDF depends on the amount of crystalline β phase, which was evaluated through FTIR spectroscopy along with the α and γ phases. The selected working conditions allow for obtaining high β phase content, about 94%. Furthermore, the overall crystallinity of the polymeric membranes, obtained by DSC, is also high, around 70%. The ESP process of PVDF is stable, allowing fibres deposition to last several hours, and to obtain various membrane thicknesses, from about 90 to 250 µm. The mechanical properties of the obtained membranes are comparable to the ones of other synthetic materials employed for cardiovascular surgery, with Young's modulus of about 40 MPa and tensile strength of around 8.4 MPa, considering membranes thick about 100 µm. The contact angle is around 115°, as expected by a hydrophobic polymer. In preliminary trials for the incorporation of MSN, 5 %vol of MSNs was added to the PVDF solution. The nanoparticles were successfully embedded into the fibres, which showed smaller diameters with respect to fibres without MSNs due to the increased viscosity of the hybrid formulation. The PVDF+MSN membrane is a promising platform for the development of the REBORN patch and the treatment of heart failure due to MI. Future work will focus on the optimization of the ESP parameter and the investigation of drug release upon ultrasound stimulation.

References

[1] M.R. Gomes, F. Castelo Ferreira, P. Sanjuan-Alberte, Biomater. Adv. 137 (2022) 212808.

[2] B. Azimi, M. Milazzo, A. Lazzeri, S. Berrettini, M.J. Uddin, Z. Qin, M.J. Buehler, S. Danti, Adv. Healthc. Mater. 9 (2020) 1901287.

[3] J. Khao-iam, A. Salea, S. Chaipo, C. Putson, J. Phys. Conf. Ser. 2431 (2023) 012003.