SCIENTIFIC AND TECHNICAL REPORT

Program 2: Increasing the competitiveness of the Romanian economy through research, development and innovation
Subprogram 2.1. Competitiveness through research, development and innovation
Project type: Experimental – demonstration project – PED
Project title: Improved technologies for the development of electrospun polysulfonic membranes integrated in an extracorporeal device applicable in renal failure
Contract no: 579PED/2022
Project code: PN-III-P2-2.1-PED-2021-2700
Project acronym: TechMembrEID
Coordinator: "Petru Poni" Institute of Macromolecular Chemistry, Iasi
Partner: Politehnica University of Timişoara
Project director: Dr. Anca Filimon

Stage 3 (2024) – Validation/testing and demonstration of the functionality of the EID device with integrated FHMs membranes

Reporting period: January – June 2024

Activity 3.1 - Demonstration of the FHMs membranes functionality for medical applications

Activity 3.2 - Evaluation of the plasma level of reactive oxygen species

Activity 3.3 - Hemocompatibility tests

Activity 3.4 – Dissemination

Summary of the stage

According to the project implementation plan/activity schedule, the current stage, **Stage 3/2024**, includes research on the functionality and performance of bioactive electrospun membranes based on quaternized polysulfone, FHMs, used as separation media in the extracorporeal innovative device (EID), to ensure the effective dialysis control and treatment.

Taking into account the aim and the proposed objectives, regarding the determination of the membranes efficiency obtained in the processes of the renal failure treatment, within the **activity 3.1 of experimental development type** (partially realized in the previous stage of **activity 2.7/2023**), the research continued and the operating parameters of the EID using the FHMs membranes obtained from the polymeric systems consisting of polysulfone with quaternary ammonium groups (PSFQ)/cellulose acetate phthalate (CAP)/polyvinylidene fluoride (PVDF) with embedded antioxidants and immobilized heparin were optimized, through

permeation experiments/dialysis processes, achieved by monitoring the main components in the simulated biological leachate (urea, creatinine, uric acid, B12).

In order to remove/eliminate the harmful effect of free radicals produced during the hemodialysis therapy, within the **activities 1.1 and 1.2 (Stage 1/2022)**, through the proposed methodology, new membrane materials (bioactive electrospun membranes, FHMs) with increased efficiency in medical therapies were designed/formulated, for which, in **activity 3.2 of the experimental development type** the evaluation of the antioxidant capacity/stability was followed. The objective to detect the level of reactive oxygen species (ROS)/oxidative stress have represented an additional experiment considering the more detailed investigation of the totoxicity/biocompatibility of the obtained membranes with impact in the dialysis process.

The materials used in devices that come into contact with blood, for example hemodialysis membranes, vascular prostheses, intravenous catheters, blood transfusion sets, require the evaluation of compatibility with blood, since often, in medical practice, the materials can be incompatible with blood and they can either affect the blood cells, causing hemolysis or can activate coagulation pathways as result of the protein adsorption. In this context, within the **activity 3.3 of experimental development type**, the functionalized FHMs membranes were tested both for the thrombogenic effect through immersion in simulated biological plasma fluid and by analysis of the proteins adsorption on the surface, and hemolytic effect, by incubating the membranes with integral blood and evaluation of the hemoglobin concentration. In addition, the morphological assessment of blood cells is an indicator that suggests a normal state of health and the absence of obvious pathologies in the absence of morphological changes.

Within the **activity 3.4 of support type**, the scientific results were disseminated, materializing in **3 ISI scientific papers (1 published and 2 sent for publication), 1 patent application and 2 papers presented at international conferences**. Also, **1 bachelor thesis** was developed/coordinated (results visible on the TechMembrEID project website <u>https://icmpp.ro/techmembreid/</u>).

All the activities provided in the implementation plan of the PN-III-P2-2.1-PED 2021-2700 project, financing contract no. 579PED/2022 for stage 3/2024 were realized.

ISI papers:

- A. Filimon, D. Serbezeanu, A.M. Dobos, M.D. Onofrei, A. Bargan, D. Rusu, C.M. Rimbu, Electrospun membranes based on quaternized polysulfones: Rheological properties– electrospinning mechanisms relationship, *Polymers*, 16, 2024, 1503. <u>https://doi.org/10.3390/polym16111503</u>
- E. Perju, D. Serbezeanu, M. Homocianu, M. Avadanei, T. Vlad-Bubulac, Differential insights into structural dynamics and photophysical behavior of two phosphorus containing diesters, *New J. Chem.* 2024, DOI: 10.1039/d4nj01844c

- 3. L. Lupa, A.M. Dobos, D. Serbezeanu, D. Rusu, D. Suflet, A. Filimon, Performance and functionality of the polysulfone electrospun membranes in hemodialysis: Control and evaluation of the surface and permeation properties, *Mater. Des.*, **2024** (in evaluation)
- 4. A. Filimon, D. Serbezeanu, I. Roșca, D. Peptanariu, M.D. Onofrei, V.Bălan, Biological response of the electrospun membranes based on functionalized polysulfones for application in renal failure: *In vitro* cytocompatibility and blood compatibility, *Biomaterials*, **2024** (in evaluation)

Scientific manifestations

- A.M. Dobos, D. Serbezeanu, D. Rusu, M.D. Onofrei, A. Bargan, A.-M. Macsim, L. Lupa, A. Filimon, Bioactive fibrous membranes based on polysulfones: Evaluation of the surface and permeation properties, *Congresul Internațional al Universității "Apollonia" din Iași, Pregătim viitorul promovând excelența*, Ediția a XXXIV-a, Iași, România, 29 februarie -3 martie 2024 (**poster**)
- D. Serbezeanu, I. Rosca, D. Peptanariu, M. Aflori, A. M. Dobos, O. Dumbrava, A. Filimon, Performance of the polysulfonic fibrous membranes in biomedical applications: Cellmaterial interaction and antimicrobial activity, *Congresul Internațional al Universității* "*Apollonia" din Iași, Pregătim viitorul promovând excelența*, Ediția a XXXIV-a, Iași, România, 29 februarie - 3 martie 2024 (**poster**)

Patent application:

A. Filimon, D. Serbezeanu, A.M. Dobos, M.D. Onofrei, D. Peptanariu, L. Lupa, *Procedeu de obținere a membranelor fibroase pe bază de polisulfonă cuaternizată funcționalizate cu antioxidanți și heparină aplicabile în procesul de hemodializă*, No. 2601/17.06.2024

Bachelor thesis (2024):

Testarea membranelor semipermeabile în procesul de îndepărtare a ureei, creatininei, și acidului uric, author: Lorena Drăgănescu, Scientific coordinators: L. Lupa, A. Filimon

Project manager,

Dr. Anca Filimon