FUNDING PROGRAMME: PNCDI III-Program P2

Increasing the competitiveness of the Romanian economy through research, development, and innovation

EXECUTIVE AGENCY FOR HIGHER EDUCATION, RESEARCH, DEVELOPMENT AND INNOVATION FUNDING

SUBPROGRAM 2.1: Competitiveness through research, development, and innovation **– Demonstration Experimental Project** – **PED**

TITLUL PROIECTULUI/ACRONIM: Innovative medical device for emergency and operational medicine, CellMATRIX

CONTRACT NO.: 496PED / 2020

TOTAL PROJECT BUDGET: 660.00 LEI **INCDTP'S BUDGET:** 220.000 LEI

PROJECT STARTING DATE: 23.10. 2020 **PROJECT ENDING DATE:** 23.10.2022

PAGINA WEB: www.cellmatrix.ro

PARTNERS:

Coordinator: Institutul National de Cercetare Dezvoltare pentru Textile si Pielărie- INCDTP Bucureşti

Partner I: Institutul National de Cercetare-Dezvoltare Medico-Militara „Cantacuzino"

Partner II: SANIMED International Impex SRL

GENERAL OBJECTIVE:

Design, development, and validation of an innovative demonstrative model as a medical device represented by a multilayer matrix for haemostasis and gunshot wounds.

OG1: Use of the knowledge generated in fundamental research efforts carried out at the level of the partner organisations to move to a higher technological maturity level (demonstrator, laboratory validated technology);

OG2: Increase the capacity of the partner research organizations (INCDTP and CCSMM) to generate validated solutions in the laboratory for new products and technologies and to offer them to SC SANIMED SA.

SPECIFIC OBJECTIVES:

OS1: To substantiate the new technological solutions for the development of medical devices for tissue regeneration dedicated to emergency and operational medicine.

OS2: To design the functionalised multilayer matrix for haemostasis and connective tissue regeneration.

OS3: To develop a new innovative medical device for haemostasis and connective tissue regeneration.

OS4: To evaluate the functionality and biocompatibility of the developed medical devices according to the requirements of the certification entities.

OS5: To optimise the technological solution for the functionalization of the surfaces of medical devices.

NOVELTY ELEMENTS/ SCIENTIFIC CONCEPT:

Main innovative aspects:

- ✓ novel surface-engineered nanomaterials aiming at the development and implementation of innovative concepts for the generation of nanoarchitectures/nanochemistries on the surface of the newly developed textile substrate, which combine different functionalities. The key action will be the development of the nanoscale fibrous mats with controlled pore size and structure, from both natural and synthetic origin polymers.
- ✓ extending the range of antibacterial elements and functionalisation of the electro spun wound dressings with active compounds that accelerate wound healing and tissue regeneration;
- ✓ development of new models and protocols for in vitro and in vivo studies of interface processes, cell biological and microbiological response.

EXPECTED EXPLOITABLE RESULTS:

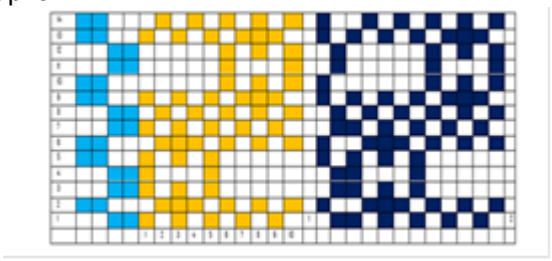
- ✓ Technological report that will fundament the most performant technologies for functionalisation of the

multilayer structure surfaces with different physical-chemical characteristics; chemical and mechanical compatibility of the substrates; biomedical and bio functional requirements and barriers in technological development; surface modification techniques specific to each substrate made of resorbable and/or non-resorbable polymers; clinical risks associated to haemostasis and connective tissue regeneration specific to burns and gunshot wounds; prevention methods etc.

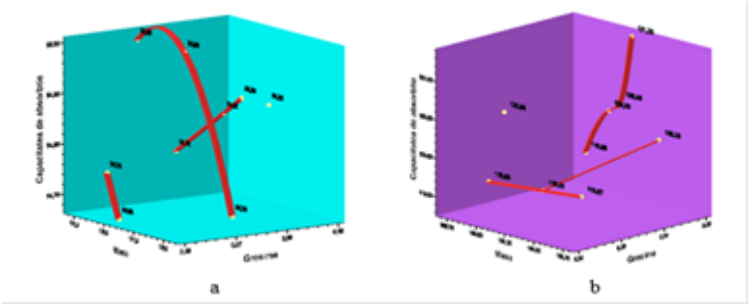
- ✓ Experimental report based on mechanical, chemical, and structural determinations for the raw materials and bioactive polymers.
- ✓ Experimental design report that will provide both the design solution of the medical device based on CAD design and FEM simulation of the multilayer structure behaviour, and the most important technological parameters.
- ✓ Various textile supports developed for the first layer of the matrix;
- ✓ Hydrogel substrates that will represent the second layer and will be deposited through different techniques onto the textile materials that will be functionalised with bioactive biological polymers and will contact the blood and damaged tissue;
- ✓ Coated substrates that represent the third layer of the matrix and will ensure the impermeability of the matrix to the bacteria;
- ✓ Medical device based on a multilayer matrix for haemostasis and connective tissue regeneration;
- ✓ The evaluation report of the medical device's level of performance;
- ✓ Technology for the DM accomplishment.

OBTAINED RESULTS :

- ❖ **3 variants of flat structures made using unconventional techniques**, differentiated by the nature of the raw material. The statistical indicators of the defining variables for each variant of textile structures were calculated, and histograms, box plot graphs, and interactive spatial graphs were drawn in the form of strip graphs.

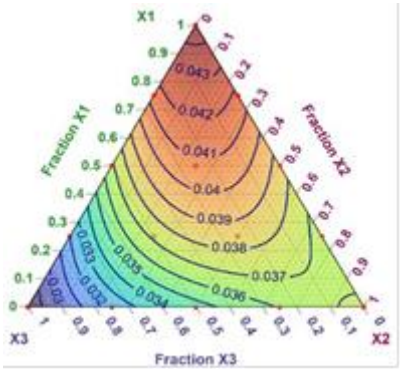


Programming scheme of the honeycomb connection



Strip graphs

- ❖ **Hydrogel-based substrates** based on an experimental plan with correlated factors, of the lattice simplex type A{q, m}, with three factors (q = 3) and four discretization intervals on the axes of the major simplex (m = 4).



Ternary diagram

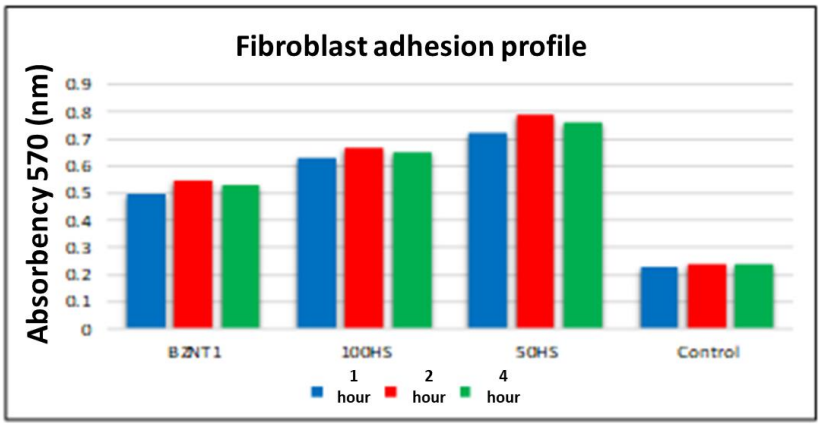
- ❖ **Impermeable substrate of the medical device** (the one that comes into intimate contact with the lesion).

It was made using the same types of textile materials as the outer layer (with the role of mechanical support) and the selection was made based on the analysis of the physical-mechanical and antimicrobial characteristics.

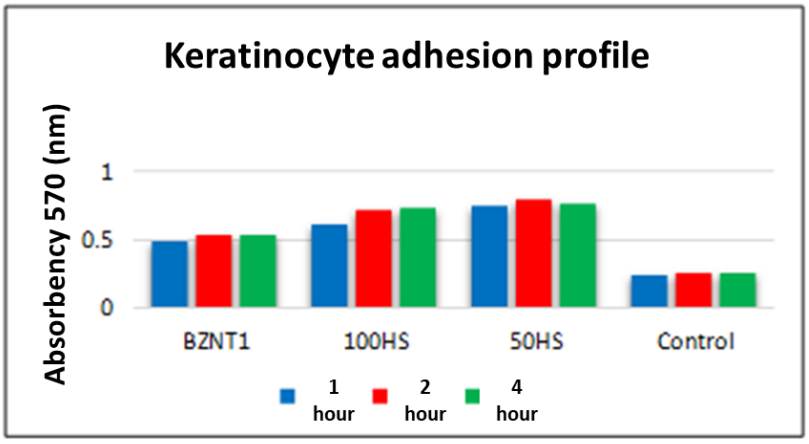
Stratified matrix

❖ **Evaluation of the antimicrobial activity** of textile structures intended for layer 1 and 3 by using standardized strains: *Staphylococcus aureus* ATCC 6538, *Escherichia coli* ATCC 8739, and *Candida albicans* ATCC 10231. The most effective antibacterial effect was obtained for cotton or Tencel structures containing Chitosan.

❖ **Cell adhesion study**. To establish the ability of a biomaterial to serve as a substrate for a cell culture, the cell adhesion efficiency must first be evaluated. The adhesion of 2 types of cells, fibroblasts and keratinocytes, to 3 test samples was evaluated, and the results were represented and compared graphically with the control, untreated coverslide.



Average values of absorbance readings at 1, 2, and 4



Average values of absorbance readings at 1, 2 and 4 hours (keratinocytes)

❖ **Cell proliferation study**. Fibroblast and keratinocyte proliferation was analyzed at 24, 48 and 72 hours of substrate-cell interaction. The increasing number of the two cell types used for viability testing of the 3 tested samples shows the occurrence of proliferation in all these models. The dynamics of cell proliferation over time, it

increases directly proportionally to the increase in the substrate-cell contact period.

❖ ***In vitro* study for testing the biocompatibility** of 3 functionalized multilayer matrices using MTT {3-(4,5-dimethyazol-2-yl)-2,5-diphenyl tetrazolium bromide}. It is a sensitive, quantitative and reliable colorimetric test that measures cell viability, proliferation and activation. In living cells, the yellow, water-soluble MTT is reduced to a dark blue formazan product by the mitochondrial dehydrogenase enzyme. The amount of formazan produced is directly proportional to the number of viable cells present. Therefore, measuring the optical density helps determine the amount of formazan produced and thus the number of viable cells present.

❖ **Demonstrative models of multi-layer devices**

Day 1 Day 3 Day 7 Day 10

Evolution over time of treated wounds

DISSEMINATION, PATENT APPLICATIONS, AWARDS:

SCOPUS published papers:

✓ **Razvan Scarlat, Catalin Grosu, Mihaela Jomir, Carmen Mihai, Alexandra Ene,** Diana Popescu, Radu-Gabriel Hertzog, *Statistical analysis of yarn characteristics for multilayer fabric matrix meant for hemostasis and tissue regeneration,* Industria Textila, vol.73, nr 4, 2022, pag. 447-453

BDI published papers:

✓ **Ene Alexandra, Mihai Carmen, Scarlat Razvan, Grosu Catalin,** Hertzog Radu-Gabriel, Popescu Diana, *New paradigms in designing the medical textiles,* ANNALS OF THE UNIVERSITY OF ORADEA, FACULTY OF TEXTILES, LEATHERWORK, vol.22, pp.37-42.

✓ **C. Mihai, A.G. Ene,** R.-G. Hertzog, D. Popescu, **A.F. Vladu** *"Predictive mathematical model for absorbent substrate achievement, through electrospinning proces**s**"* Proceedings of International Conference TexTeh X, pag.355-362, DOI: 10.35530/TT.2021.59, CrossRef and Index Copernicus indexed

✓ **Alexandra Gabriela Ene, Carmen Mihai, Emilia Visileanu,** Radu-Gabriel Hertzog, Diana Popescu, **Alina Vladu** ,"*Descriptive statistics for planar multilayer matrix structures for hemostasis and tissue regeneration*" Industria Textila, ISSN 1222-5347 Science Citation Index Expanded (SCIE), Materials Science Citation Index®, Journal Citation Reports/Science Edition, World Textile Abstracts, Chemical Abstracts, VINITI, Scopus, Toga FIZ technik, EBSCO, ProQuest Central, Crossref ISI indexed-vol.73, nr. 3, pag. 288-294, 2022 http://doi.org/10.35530/IT.073.03.202139

Scientific communications:

✓ **Ene Alexandra, Mihai Carmen, Scarlat Razvan, Grosu Catalin,** Hertzog Radu - Gabriel, Popescu Diana, *New paradigms in designing the medical textiles,*21st International Conference "Innovative solutions for sustainable development of textiles and leather industry", Oradea, May 21- 22, 2020

✓ **C. Mihai, A.G. Ene,** R.-G. Hertzog, D. Popescu, **A.F. Vladu** *"Predictive mathematical model for absorbent substrate achievement, through electrospinning process"* C. Mihai, A.G. Ene, R.-G. Hertzog, D. Popescu, A.F. Vladu, International Conference TexTeh X, Bucharest, Romania, 21-22.10.2021, online.

Patent Applications: Procedure for obtaining layered dressings, usable for assisting medical interventions performed in emergencies, **Visileanu Emilia, Ene Alexandra Gabriela,** Popescu Diana Mihaela, Maier Stelian Sergio, Tihauan Bianca Maria, Marinas Ioana Cristina, A/00612106.10.2022

Awards: Gold Medal-International Exhibition INVENTCDR 5th edition, 3-5 April 2025, Deva, Romania

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Information Technology in Industrial Engineering Research Department