

This study was funded by the National Research Authority through the Nucleu Program project PN 23 26 03 01 - Advanced and sustainable polymer biocomposites for the footwear industry and niche areas made according to the principles of the circular economy (AVANS-COMP-POLYMER)

FUNDING PROGRAMME: UEFISCDI Executive Agency for Higher Education, Research, Development and Innovation Funding



SUBPROGRAMME: Partnerships for Competitiveness - PED Demonstration Experimental Project, 2021 competition

PROJECT TITLE/ACRONYM: Design, modeling and validation of novel biohybrid for wound healing applications by tissue engineering/ HEALSKIN

CONTRACT NO.: PED 622 / 2022

TOTAL PROJECT BUDGET: 598.795 lei

INCDTP'S BUDGET: 250.000 lei

PROJECT STARTING DATA: 23/06/2022

PROJECT ENDING DATA: 20/06/2024

WEB PAGE: <https://sorinadinescu.wixsite.com/622pedhealskin>

PARTNERS:

► CO: University of Bucharest, Faculty of Biology, Department of Biochemistry and Molecular Biology, Research Platform in Biology and Systems Ecology (PCBE), Project director: Assoc. Prof. Sorina Dinescu, PhD



► Partner: National Research and Development Institute for Textile and Leather (RO) - Project Responsible: Dr. Mădălina Albu-Kaya



GENERAL OBJECTIVES:

The aim of HEALSKIN project is to develop and validate at lab scale an innovative biohybrid with multiple therapeutic properties for chronic wound healing applications, based on natural components (collagen, sericin) and improved with two flavonoids (curcumin and quercetin).

SPECIFIC OBJECTIVES/ EXECUTION PHASES:

Objective 1: Synthesis of key elements necessary for the material's elaboration;

Objective 2: Development of the hybrid biomaterial with pro-regenerative, anti-inflammatory, antioxidant and pro-angiogenic properties;

Objective 3: Demonstration of the effectiveness of the biohybrid with a role in the regeneration of damaged cutaneous tissue.

NOVELTY ELEMENTS/ SCIENTIFIC CONCEPT:

The project has been focused on developing novel therapeutic approaches for different types of wounds. In this regard, an improved method of treatment would be the topical application of therapeutic agents with multiple properties (anti-inflammatory, antioxidant, antimicrobial, pro-angiogenic, pro-regenerative) that could facilitate the impaired healing process of such lesions.

EXPECTED EXPLOITABLE RESULTS:

Phase I/2022

- experimental data set regarding: obtaining precursors: collagen type I, curcumin, quercetin and microcapsules;
- obtaining cross-linking agent and characterization report;
- report regarding the cytocompatibility of precursors with skin-specific cells;
- development of project website;
- 1 intermediate research report.

Phase II/2023

- experimental data set regarding the characterization of HEALSKIN compositions, biocompatibility of the optimally chosen hybrid, cell adhesion, inflammation markers and antioxidant markers;
- updating the project website;
- 1 intermediate research report;

- 2 scientific communications at conferences;
- 1 ISI article.

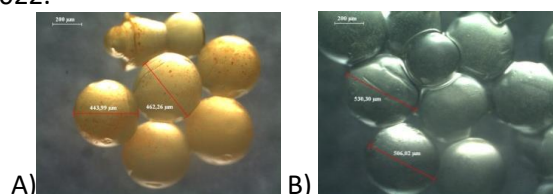
Phase III/2024

- report of HEALSKIN biomaterials biodegradability;
- experimental data set on antibacterial properties, proangiogenic markers and extracellular matrix markers;
- website update;
- 1 final research report;
- 2 scientific communications at conferences;
- writing an article for submission;
- a patent application registered at OSIM.

OBTAINED RESULTS:

Results Stage I / 2022

- ✓ precursors were obtained and characterized (type I collagen gel from bovine skin; sericin, curcumin and quercetin microcapsules, new aldehyde crosslinking agents) [A1.1- 1.3, A1.5];
- ✓ the effect of microcapsules and crosslinking agents on skin cells of interest (viability profiles) was identified [A1.4., A1.6];
- ✓ a website, and the results were also disseminated by participating with an invited paper at a specialized conference;
- ✓ scientific report for stage I / 2022.



A) B)
Collagen microcapsules with a) curcumin and b) quercetin

Results Stage II / 2023

- ✓ data were obtained regarding the physicochemical, morphological and structural characterization of HEALSKIN compositions [A2.1, A2.2, A 2.5];
- ✓ biocompatibility was validated and the optimal composition to support skin cell viability and proliferation (CollSS-CQ) was identified [A2.3, A2.4, A2.6];
- ✓ cytoskeletal changes were highlighted in the presence of the HEALSKIN composite, with skin cells having an elongated morphology at the level of this material [A2.7];
- ✓ gene and protein expression of the pro-inflammatory markers IL-6 and TNF- α was evaluated, and HEALSKIN showed an anti-inflammatory effect [A2.8];
- ✓ at the level of the HEALSKIN composite, a reduction in ROS production was found, indicating its antioxidant effect [A2.9];
- ✓ website updated with the results of stage II
- ✓ scientific report for stage II/2023;
- ✓ 3 scientific communications at conferences;
- ✓ 1 ISI article published.

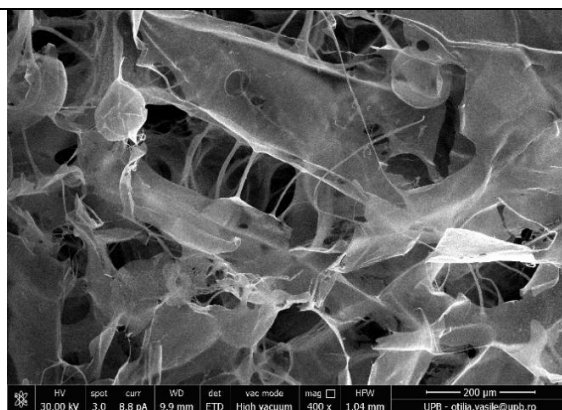


Coll-SS-MC-4C



Coll-SS-MC-3Q

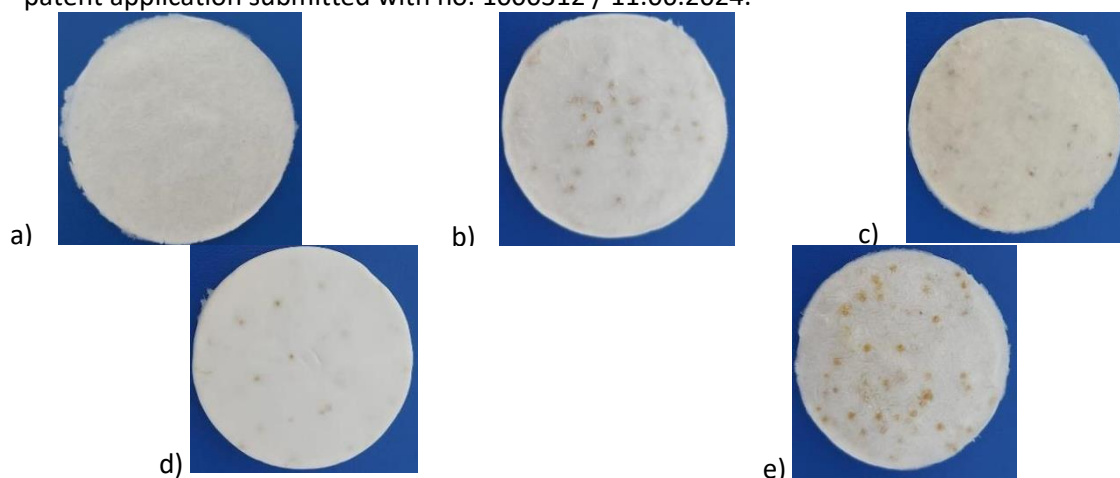
HEALSKIN collagen-sericin matrices with encapsulated curcumin and quercetin



SEM images (400x magnification) for the HEALSKIN matrix with embedded microcapsules

Results Stage III / 2024

- ✓ data on HEALSKIN biodegradability were obtained [A3.1];
- ✓ the HEALSKIN composite showed antimicrobial activity [A3.2] - gene and protein expression of angiogenic markers - VEGFR2 and CD31, as well as markers specific to the extracellular matrix - fibronectin and collagen type IV, increased significantly at the level of the HEALSKIN composite, as a result of flavonoid encapsulation, which indicates the potential of the material to facilitate the skin regeneration process [A3.3, A3.4];
- ✓ website updated with stage III results;
- ✓ scientific report for stage III/2024;
- ✓ 4 scientific communications at conferences;
- ✓ 1 ISI article published;
- ✓ patent application submitted with no. 1000312 / 11.06.2024.



Scaffold-uri CollSS: a) uncrosslinked; b) crosslinked with GA; c) crosslinked with GE; d) crosslinked with EU and e) crosslinked with CM

DISSEMINATION, PATENT APPLICATIONS, AWARDS:

• WoS published papers:

1. Tudoroiu, E-E., Albu Kaya, M. G., Titorencu, I., Dinu-Pîrvu, E-C, Marin, M.M., Roșca, AM., Popa, L., Anuța, V., Antoniac, A., Chelaru, C., Kaya, D.A., Prisada, R., Ghica, M.V., Design and evaluation of new wound dressings based on collagen-cellulose derivatives, *Materials & Design*, 236, 2023, 112469. [ISI 8,4; Q1], WOS WOS:001116308400001.
2. Sleiman, L.; Lazăr, A.-D.; Albu-Kaya, M.; Marin, M.M.; Kaya, D.A.; Vasile, O.-R.; Dinescu, S., 2024. Development and Investigation of an Innovative 3D Biohybrid Based on Collagen and Silk Sericin Enriched with Flavonoids for Potential Wound Healing Applications. *Polymers*, 16, 1627. [ISI 5,0; Q1], WOS WOS:001256663400001.

• Scientific communications:

1. Albu Kaya M., Collagen – Biomaterial for Health, BeHEALTH 2022, Online International Event in Healthcare!, 25-27 octombrie 2022. Virtual
2. Dinescu S., Lazar A.D., Marin M.M., Albu-Kaya M.G., Costache M, Biocompatibility assessment and

cytoskeleton development of human skin cells in contact with a novel biohybrid loaded with curcumin and quercetin for potential wound healing applications, 47th FEBS Congress, 8-12.07.2023, Tours, Franța.

3. Lazăr (Popa) A.D., Sleiman L., Marin M.M., Albu-Kaya M.G., Costache M., Dinescu S., Novel biohybrid enriched with curcumin and quercetin displays favorable properties as potential active wound dressing for biomedical applications, The Annual International Conference of RSBMB, 13-15.09.2023, Cluj-Napoca, România.
 4. Albu Kaya M., Multiparticulate delivery systems based on collagen and anti-inflammatory drugs, BeHEALTH 2023, Hybrid International Event in Healthcare, 24-26.10.2023, Timișoara, România.
 5. Lazăr (Popa) A.D., Sleiman L., Marin M.M., Albu-Kaya M.G., Dinescu S., Novel biohybrid loaded with curcumin and quercetin displays proangiogenic potential for prospective wound healing applications. Tissue Engineering and Regenerative Medicine (TERM-2024) Conference, 11-12.06.2024, Virtual.
 6. Albu Kaya M.G., Collagen-sericin biohybrids for tissue engineering, International Symposium on Biomass Resources and Materials, 25-28.03.2024, Zhengzhou, China.
 7. Sleiman L., Lazăr A.D., Zarnescu O., Dinescu S., Evaluarea efectului reglator al curcuminei asupra procesului de diferențiere adipogenică a celulelor stem izolate din țesut adipos. Sesiunea de Comunicări Științifice a Studenților Facultății de Biologie, 17.05.2024, București, România.
 8. Tudoroiu E.E., Ghica M.V., Albu Kaya M.G., Dinu-Pîrvu C.E., Popa L., Titorencu I., Udeanu D.I., Anuța V., Marin M.M., Prisada R.M., Design, evaluation and optimization of new collagen-hydroxyethylcellulose wound dressings loaded with naproxen, Congressus Pharmaceuticus Hungaricus (CPH) XVII and EUFEPS Annual Meeting, 23-25.05.2024, Debrecen, Ungaria.
- **Patent Applications:** Agent natural de reticulare a colagenului și procedeu de obținere a acestuia, autori: Albu Kaya M.G., Marin M.M., Kaya D.A., Ignat M.C., patent application no. A 100312/11.06.2024.
 - **Awards:** Gold medal for inovation: Agent natural de reticulare a colagenului și procedeu de obținere a acestuia, autori: Albu Kaya M.G., Marin M.M., Kaya D.A., Ignat M.C., poster presented at National Salone of Inventions and Inovations „Traian Vuia”, Timișoara, 13-15 June 2024.

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