GROUP OF BIOMATERIALS (Institute of Polymer Science and Technology, ICTP-CSIC; http://www.biomateriales.ictp.csic.es/en/biomaterials-group/)

PIF2024 - REGULATION OF OXIDATIVE STRESS AND CONTROL OF INFLAMMATORY MICROENVIRONMENT WITH INNOVATIVE BIOMATERIALS (ROSCON), PID2023-149301OB-I00

Previous results of the team in the theme of the proposal.

Over the past 20 years, one of the primary researches focuses of our team has been the **conjugation of bioactive compounds**, including antioxidants, anti-inflammatory drugs, and antibiotics, with both natural and synthetic polymers. This research line has been a part of various national projects (**MAT2007-63355, MAT2010-18155, MAT2014-51918-C2-1-R, MAT201573656-JIN, MAT2017-84277-R, and PID2020-114086RB-I00**), projects supported by the Health Institute Carlos III through CIBER-BBN, as well as international projects (**HORIZON-MSCA-2022-SE-01**). In the last two national projects, our team has gained significant expertise in conjugating catechol moieties to resorbable synthetic polymers, employing and optimizing various conjugation strategies (1–4). Some of these conjugates are currently being applied in promising new developments with the potential for translation to clinical applications, as part of a public-private collaboration project with Aerofybers (**CPP2022-010024**).

Furthermore, our team possesses substantial experience in **engineering scaffolds** using natural polymers such as HA, gelatine, chitosan and alginate. Various crosslinking methods and synthetic routes (covalent and electrostatic interactions) have been explored, as evidenced by the outcomes of the aforementioned national projects. A related area of interest for our team involves the development of **controlled drug delivery systems**, including NPs for the controlled release of bioactive compounds such as antioxidants, anti-inflammatory drugs, and antibiotics. Specific contributors to this research include (1,5–8)

In terms of **support design**, our team has explored a range of systems, including semi- and Interpenetrating polymer network hydrogel systems (2,4), electrospun meshes (9), 3D bioprinted scaffolds (10,11), and bioactive viscosupplements (12). Notably, recent developments include hydrogels applicable in osteoarthritis (13), which entrapped anti-inflammatory drugs like dexamethasone, showing potential in cartilage repair (14).

Regarding the chosen **final applications**, Dr. María Rosa Aguilar (PI1) has supervised two PhD theses on wound dressings (Dr. Felisa Reyes, 2013) and bioactive viscosupplements (Dr. Gloria Pontes, 2021), both resulting in high-impact scientific articles. Additionally, PI1 is the coordinator of a CAM Biomedicine Program since January 2023 focused on developing solutions for radiated skin treatment (RADIOPROTECT). Our ROSCON project will try to go a step further in the development of these solutions and propose **new Smart Responsive Systems (SRS)**, sensitive to oxidative stress and inflammatory microenvironment to have better control over the release of active molecules.

The **multidisciplinary nature of our team**, comprising chemists from the Biomaterials group at the Institute of Polymer Science and Technology (ICTP-CSIC) and Universidad San Pablo CEU (USPC), experts in histology and animal experimentation from the University of Salamanca (USAL), along with a clinician (traumatologist) from Hospital Ramon y Cajal (HRC), ensures the achievement of the proposal's objectives. It is noteworthy that our team has consistently delivered fruitful results and received excellent evaluations from referees in the aforementioned National projects.

In terms of **knowledge transfer**, our team has a **strong track record** of collaborating with various Spanish companies through R+D contracts (LVD Biotech, ALODIA Farmacéutica, Zoitech, Arquimea Agrotech, Viscofan…), national projects (CPP2022-010024 in collaboration with IATA-

CSIC and Aerofybers), and CIBER-BBN Transfer projects (NADEAFNESS and POLYNARED, in collaboration with ALODIA Farmacéutica) in recent years.

Human, material, and equipment resources available for the execution of the Project.

The research team is composed of 6 full-time researchers with a high level of expertise, drawn from 4 distinct research centres and universities: ICTP-CSIC, USAL, USPC and HRC. Their complementary skills and knowledge ensure the feasibility and successful execution of the project. Together, they encompass the diverse disciplines required for the project's various stages, from the synthesis and characterization of biomaterials to *in vitro* and *in vivo* functional assessments. The PIs belong to the Biomaterials Group of the ICTP-CSIC recognized for their expertise in the development of biomaterials.

- **PI1: María Rosa Aguilar** (ORCID: 0000-0001-7395-5754) is a Tenured Scientist at the ICTP-CSIC and conducts advanced research in the field of new biomaterials for drug delivery systems and tissue regeneration.
- **PI2: Luis Rojo** (ORCID: 0000-0001-6334-6736) is a Distinguish Researcher at the ICTP-CSIC and conducts advanced research in the field of biomaterials for tissue regeneration with high expertise in the field of bone and cartilage.
- **Cristina Abradelo** (ORCID: 0000-0001-7297-1357) is a University Full Professor at the USPC with a wide background in physical chemistry and polymers.
- **Lorena Benito** (ORCID: 0000-0002-4413-388X) is a Contracted Doctoral Lecturer at the Biomedical Research Centre of the USAL. She is a histologist and conducts advanced *in* vivo research to evaluate different biomaterials applications.
- **Omar García** (ORCID: 0000-0002-5145-8455) is an Assistant Lecture Doctor at the Anatomy and Histology Department of the USAL. He oversees *in vitro* and *in vivo* research of new biomaterials.
- **Basilio de la Torre** (ORCID: 0000-0001-7809-7592) is a Head of Traumatology and Orthopaedic Surgery Service at the HRC with wide expertise in biomaterials research and OA *in vivo* studies.

It is important to highlight that there is **a stable and fruitful collaboration between the researchers** of the diverse groups involved in this project, which were already teamed in previous National projects (**MAT1999-1064-C02-01, MAT2002-04147-C02-02, MAT2007-63355, MAT2010-18155, MAT2014-51918-C2-1-R, MAT2017-84277-R,** and **PID2020-114086RB-I00**) and count with several joint publications.

Regarding the equipment and the infrastructure, the ICTP-CSIC has a fully equipped chemistry laboratory for the synthesis and preparation of the different systems proposed in the project. An electrospinning equipment and a new custom-made iRJS were set up to prepare the different wound dressings. To carry out the physicochemical, thermal, and biomechanical characterization of the materials developed in the proposal the ICTP-CSIC is equipped with an FTIR, UV-VIS, liquid and solid NMR spectroscopies, Mass Spectrometry (MS), Equipment for Contact Angle Measurements, Dynamic Light Scattering (DLS), Zetasizer, Optical Microscopy, Environmental Scanning Electron Microscopy (ESEM), Transmission Electron Microscopy (TEM) coupled with EDAX, Atomic Force Microscopy (AFM), High-Resolution Liquid Chromatography (HPLC), Size Exclusion Chromatography (SEC), Surface Plasmon Resonance (SPR), DSC, TGA, X-Ray Diffraction (XRD), Universal Testing Machines (UTS), Dynamic Mechanical Thermal Analysis (DMTA), Rheometers and Quartz Crystal Microbalance with dissipation monitoring (QCM-D).

Also, the Biomaterial group is part of the SUSPLAST+ platform and has access to their infrastructure (Environmental-controlled electrospinning, TGA, DSC, HPLC, 3D printers). These equipment resources will be complemented with the resources of the USPC to study biomolecular interactions by ITC.

In vitro studies will be conducted at ICTP-CSIC and USAL. Both groups present the infrastructure and necessary equipment for *in vitro* evaluation of the biocompatibility of the developed systems. This includes different types of cell cultures and the following equipment and instrumentation: Several incubators, baths, centrifuges and laminar flow hoods, optical microscopes, epifluorescence microscopes, plate reader, shaker incubators, dewars or cryogenic refrigerators, Real-Time PCR, RNA/DNA UV Cleaner, automated cell counter, incubator chamber for live microscopy, rotary microtome, paraffin embedding station, liquid-based cytology processor.

For *in vivo* experimentation and evaluation, the anatomy and histology department of the USAL and the Department of Orthopaedic Surgery of HRC, have the necessary infrastructure to perform the necessary *in vivo* assays for the project as well as its evaluation: microtome and cryotome, systems for paraffin inclusion of samples and optical and fluorescent microscopy. Finally, the Biomaterials Group (ICTP-CSIC) is also part of the Biomedical Research Centre in Bioengineering Biomaterials and Nanomedicine (CIBER-BBN) and has preferential access to the NANBIOSIS infrastructure, a Singular Scientific Technological Infrastructure (ICTS) recently recognized by the Spanish authorities, for the production and characterization of nanomaterials, biomaterials and systems in biomedicine.

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