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POLYSACCHARIDE-BASED (BIO)HYBRID NANOSTRUCTURES

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Polysaccharide based (Bio)Hybrid Nanostructures (HYBSAC) is a project being implemented by the "*Petru Poni" Institute of Macromolecular Chemistry* (ICMPP), Iasi, Romania, project no. 760082/23.05.2023, project code CF201/28.11.2022, funded by the National Recovery and Resilience Plan, Component C9 - Support for the private sector, research, development, and innovation, Investment I3: Development of a program for attracting highly specialized human resources from abroad for research, development and innovation activities.

The goal of the HYBSAC project is to increase the competitiveness of Romanian research, at the national and international level, and build a research core with high-level scientific competence, under the coordination of an international expert, and build a new research field within ICMPP. Top methods will be addressed for synthesizing, characterizing and testing polysaccharides with synthetic polymer components using RAFT polymerization methodologies.

The HYBSAC research project aims to develop new hybrid nanomaterials that will be formed from the combination of natural polysaccharides, synthetic/soluble responsive and biocompatible polymers. The synthesis will be specifically achieved by growing the synthetic polymers in a covalent manner to polysaccharide chains using the RAFT polymerization mechanism. RAFT polymerization is a controlled radical polymerization process that allows for sophisticated tuning of both the structure and functionality of the polymer.

Two synthetic strategies were developed.

- **Grafting-from**, in which polymer grow directly from the polysaccharide backbone.
- **Grafting-to**, in which pre-synthesized polymers will be chemically attached to the polysaccharide.

Either of these approaches was obtain **hybrid synthetic-biological polymers** for advanced functional properties. We will also study the **self-assembly and co-assembly** of these hybrid materials producing well-organized nanostructures through polymer physical chemistry principles, informed by the study of these assemblies in aqueous environments and their structural features and formation mechanisms.

The resultant nanoassemblies was assessed for a variety of high-impact applications such as:

- **Drug delivery, bioimaging and protein transport.**
- **Environmental restoration** as nanocontainers for capturing organic/inorganic pollutants.
- **Surface functionalization** for high-performance material interfaces.

Furthermore, co-assembly with **proteins and antibodies** allow us to create **biofunctional nanoparticles** with biomimetic architecture for diagnostic and treatment purposes. The project also generate **hybrid organic–inorganic and bio–inorganic nanostructures** by co-assembly of functionalized polysaccharides and inorganic nanoparticles, in attempts to create materials that possess **magnetic, optical, catalytic** or **antimicrobial** properties.

The project is coordinated by Dr. Stergios PISPAS, Research Director at the Institute of Theoretical and Physical Chemistry, National Hellenic Research Foundation, Greece (TPCI/NHRF). Dr. Pispas has expertise in polymer synthesis using controlled polymerization techniques, with innovative results applicable in nanomedicine and the delivery of drugs/genes/proteins for therapy, bioimaging, detection, and water treatment. As further evidence of his scientific achievements, Dr. Pispas was included in the *Top 2% Scientists Worldwide in Chemistry* in the field of polymers for the years 2018–2022.

The project team is mainly formed by *Functional Polymers Laboratory* members from ICMPP (https://icmpp.ro/laboratories/l4/description.php), coordinated by Dr. Marcela Mihai, one of Romania's leading research groups with internationally recognized interests on multifunctional (composite) materials mainly through the synthesis and utilization of a variety of synthetic and natural ionic polymers with predetermined functional groups and architectures. In addition, two members of the HYBSAC team originate from TPCI/NHRF, as part of Dr. Pispas's team, to assist with implementing the project. Dr. Pispas' collaborations with Romanian team members date back to 2012 with a number of research visits performed at TPCI/NHRF on subjects aligned with the HYBSAC project.

The project implementation period is 60 months, from July 1, 2023, to June 30, 2026.

The total value of the financing contract is 7,551,991.04 RON, non-reimbursable funds from the European Union – NextGenerationEU, of which the non-reimbursable financing amount is 7,000,000 RON and the VAT related to eligible expenses from PNRR is 551,991.04 RON.

The **general objective** of the HYBSAC project is to increase the capacity and quality of research and development activities at ICMPP by attracting specialists with advanced skills from abroad, opening a new research direction in the field of biomaterials, and creating a research excellence group.

Specific objectives of the HYBSAC project include, but are not limited to:

- Polysaccharides containing rationally designed synthetic polymer constituents obtained by controlled RAFT polymerization. Graft copolymers made with controlled composition and structure. Structural elucidation, self-assembly, and morphology will be evaluated in aqueous media and on substrates.
- Development of biocompatible, synthetic-biological polymer constituents with temperature-triggered and pH-triggered properties that can be co-assembled with biologically relevant materials, namely therapeutic payloads, enzymes, and pre/in-situ created inorganic nanoparticles, for hierarchical control of nanostructures, responsive and environmental conditions, external stimulation, and reaction of the hybrid nanostructures to a specific environmental condition (i.e. those found in living tissue).
- Studying the external controlling/stimulating effects facilitated by the interactions of inorganic components that are responsive, e.g., light and NIR, (ex. gold nanoparticles) embedded in hybrid polysaccharides, or those controllable by an external magnetic field or other forms of radiation (for example, magnetic iron oxide nanoparticles), to regulate their enzymatic activity and analyze/evaluate the combined effects of simultaneous hyperthermic, photothermic, and photodynamic therapy for combined/synergistic therapy and diagnostics.

Specific objectives of the HYBSAC Project (***Aligned with PNRR – Pillar III Strategic Priorities***)

- Enhance the National and International Competitiveness of Romanian Research by establishing a research core with high-level performance indicators (performance center) emphasizing polysaccharide hybrid materials, which was started under the supervision of an internationally renowned researcher and expert, and a new research pathway on hybrid materials based on polysaccharides in high technology. Also, advanced RAFT polymerization techniques have been developed, which will yield polysaccharides with synthetic polymer components to determine the synthesis, characterization, and testing proportions of pure polysaccharide and hybrid polysaccharides and how much of the synthetic polymers are the same.
- Develop the International profile of ICMPP and allow for the new performance Hybrid Materials Research Core to work on EU and national research programs so that it increases the profile of the institution and becomes active in working with other studies.
- Increase the quality and specialization of the human resources by scientific training and collaborative research under different disciplines. The project will be the vehicle where world-class research will be undertaken. It can allow members of the team to acquire competencies as well as improve their practice for those researchers who have more experience in the field of the project.

The activities in HYBSAC will enhance the team knowledge in producing nanomaterials/nanostructures with more desirable properties and functions, greater diversity, and durability. This knowledge will be readily adopted in industry. The group of young researchers (Postdocs and PhD students) engaged in HYBSAC will receive training in a multidisciplinary context within a state-of-the-art research field, concerning a contemporary issue of material sustainability and ecological social development.

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