

Intelligent Polymeric Micro- and Nanoparticles for Self-regulated Drug Delivery System

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GROUP SKILLS

Team has a rich experience and is established as a leading research group in Romania and recognized abroad in the field of drug delivery systems and enzyme immobilization.

- has obtained **microgels** both from natural polymers such as starch, dextran, pullulan, alginates, and synthetic polymers such as acrylic acid, methyl methacrylate, hydroxyethyl acrylate, ethyleneglycol dimethacrylate. These microgels were prepared by various methods, with and without crosslinking agents taking under consideration the route of administration: suspension crosslinking, solvent evaporation technique, chelation, free radical polymerization of the monomers, etc.
- a long expertise in the **characterization of nanoparticles** by optical and scanning electron microscopy, inverse size exclusion chromatography, DSC, FT-IR.
- a good experience in **methodologies for validation of delivery systems**: *in vitro* release studies, pharmacokinetics, pharmacodynamics, mathematical analysis of release data.
- A rich **international experience**. They have prepared Ph.D. thesis and then, they have worked in laboratories from France and Italy. All of them are well-known through their articles published in important international journals, ISI indexed, with high impact factor, through several conferences given at international scientific events, through monographs published in international publishing houses, through conferences given as invited lectures in foreign universities or institutes. The researchers involved in the development of this project have a large professional experience in the realization of the research projects (CEEX) as director or team responsible during the past competitions such as the CNCSIS, CERES, BIOTECH, INVENT programs, etc.

COLABORATIONS

INTERNATIONAL PROJECTS awarded by competition, based on their examination by mixed juries, financed by the Ministry of Education and Research (MEC) from Romania and the homologue Ministries from partner countries.

- Bilateral cooperation between Romania and Italy, theme of the project: *Polyosaccharides based micro- and nanospheres as delivery system for drug and bioactive compounds*, 3 years (1998-2000).
- Bilateral cooperation between Romania and Italy, theme of the project: *Polymeric microparticles as delivery system for drugs and other bioactive compounds*, 4 years (2000-2004).
- Bilateral cooperation between Romania and Greece, theme of the project: *Advanced-knowledge based multifunctional materials for biotechnological and biomedical use*, 2 years (2005-2007).

PROJECTS

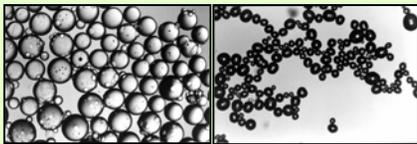
NATIONAL PROJECTS

- *Micro- and nanoparticles based on polysaccharides (alginate acid) as drug delivery systems*, 1998-2000, MEC, 1000 €.
- *Control of the human and bacterial cell interaction with NANOstructured surfaces: strategies towards "INTELLIGENT" biosurfaces*, 2006-2008, CEEX, 64000€.
- *Intelligent micro- and nanoparticles based on stimuli-sensitive polymers and/or molecularly imprinted polymers as self-regulated drug delivery systems*, Ideas Program-Exploratory Research Project, 2008-2011, 100000 €

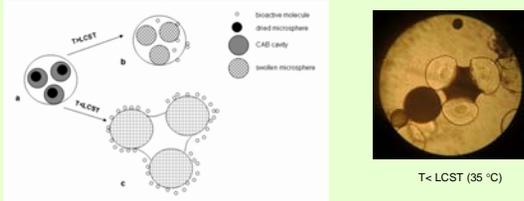
Partner in 16 national projects.

The research results obtained in the framework of these projects consist in new supports for controlled delivery of drugs. Thus, it was prepared: alginate acid microparticles for the administration of antitumor drugs (tetraamines); bioadhesive starch microspheres for nasal administration of antitumor drugs; pullulan and poly(vinyl alcohol) microspheres for controlled release of DNA, cellulose acetate butyrate microspheres for oral administration of tetraacycline. It was created new concepts such as multicompartimental devices as self-propelled drug delivery systems or intelligent systems for drug transport to the colon.

Intelligent Implantable Microcapsules for Persons that work in dangerous cold places (i.e. climbers)

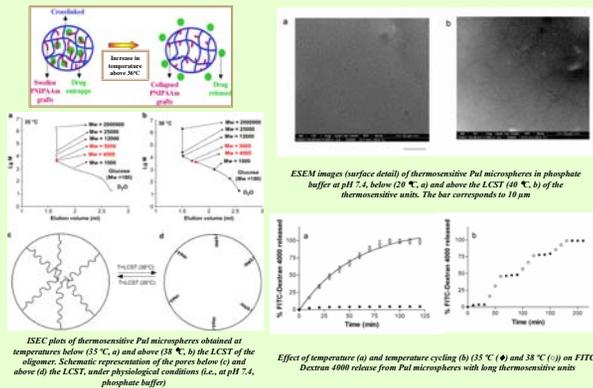


Intelligent starch microspheres below (left) and above (right) the LCST



Schematic representation of an intelligent implantable microcapsule in the dried state (Panel a), drug release from the encapsulated microspheres in the swollen state in physiological conditions (PB at pH = 7.4) above LCST (Panel b) and below LCST (Panel c).

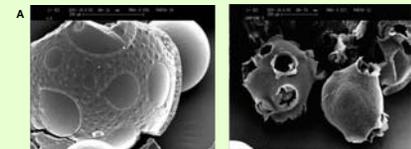
Entrapment and release of drugs by a strict "ON-OFF" mechanism in pullulan microspheres with pendant thermosensitive groups



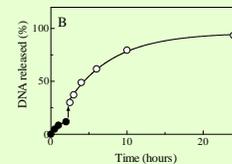
ISEC plots of thermosensitive Pst microspheres obtained at temperatures below (35 °C, a) and above (38 °C, b) the LCST of the oligomer. Schematic representation of the pores below (c) and above (d) the LCST, under physiological conditions (i.e., at pH 7.4, phosphate buffer)

Effect of temperature (a) and temperature cycling (b) (35 °C (●) and 38 °C (○)) on FITC-Dextran 4000 release from Pst microspheres with long thermosensitive units. The bar corresponds to 10 μm

Intelligent microcapsules for delivery of DNA to the colon

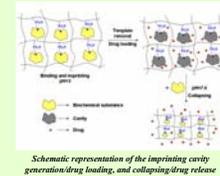


Scanning electron photomicrographs of cellulose acetate butyrate/intelligent polymer microcapsules before (A) and after (B) incubation in phosphate buffer at pH = 7.4, T = 37 °C.

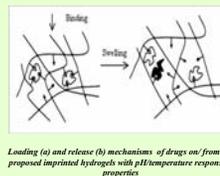


DNA release profile from encapsulated PVA microspheres after incubation in acidic buffer at pH 1.2 for 2 h, and then transferred in isotonic phosphate buffer, pH 7.4

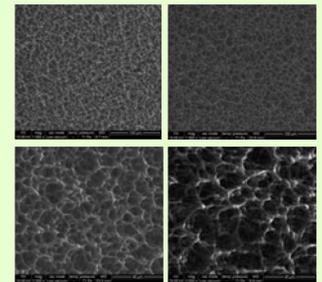
New generation of drug delivery device based on a sensor able to detect the perturbation of the normal physiological conditions and a delivery component that release the necessary dose of drug



Schematic representation of the imprinting cavity generation/loading, and collapsing/drug release



Loading (a) and release (b) mechanisms of drugs on from the proposed imprinted hydrogels with pH/temperature responsive properties



ESEM images of imprinted thermoresponsive polymer microspheres (surface detail)

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ACKNOWLEDGEMENTS

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