Project tytle:

"Interdisciplinary research on multi-functional hybrid particles for bio-requirements”

acronym: INTERBIORES

Contract no. 211/2012

Project Cod: PN-II-PT-PCCA-2011-3.2-0428 – Program PN II – Partnerships Priority Areas - Applied Research Projects – Type 2

Contracting Authority: Executive Unit for Financing Higher Education, Research Development and Innovation (UEFISCDI)
Contractor: "Petru Poni" Institute of Macromolecular Chemistry, Iasi

- Duration of project: 02.07.2012 – 02.07.2015
- The total value of the contract 3.323.334 lei
- From the source of funding:

Source 1 - The state budget: 2.950.000 lei

Source 2 - from other sources

(Net financing) 373.334 lei

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Abstract

- The project with multi-disciplinary character is focused on analysis and solving from the physical, chemical and biochemical viewpoint the design and technology of novel systems, based on antioxidants-loaded core-shell magnetic nanocomposites deposited onto the stent surface. Novel formulation methods based on the use of biocompatible polymers will be developed and applied to create a family of magnetic nanoparticles (MNPs) further characterized as a platform for magnetically guided delivery of therapeutics. The selected polymers will undergo physical (forming of interpolymer complexes by physical interactions) and chemical (functionalization, derivatization, crosslinking, reactive mixing) modifications in order to obtain stable multifunctional nanosystems. The key features of the new target delivery systems will be investigated, including *in vitro* bioactive compounds activity, capacity to protect the antioxidants from proteolysis, as well as the capacity of the magnetic guidance and retrieval. The project includes aspects like toxicology, biocompatibility of the nanodevices, and also efficacy and biodistribution of the system. The studies are doing to the facts that a major problem associated with target delivery is the inability to deliver pharmaceuticals to a specific site of the body without causing nonspecific toxicity. The bioproducts loaded magnetic nanoparticles have several advantages such as: small particle size, large surface area, magnetic response, biocompatibility and non-toxicity and are directed with external magnets to the right site, and requires smaller dosage because of targeting, with no side effects.
- One of the most innovative aspects of this proposal is the use of functionalized magnetic nanoparticles with antioxidative biomolecules deposited onto the stent surface to realize a drug-eluting-stent type for bio-requirements. The new stent device will functioning as a delivery platform. At the same time, the prepared MNPs will represent a particularly appropriate tool based on their ability to be simultaneously functionalized and guided by an external magnetic field, the presence of the antioxidative biomolecules would be an additional benefit.
- To conclude, the purpose of the multi-disciplinary character project is to realize target delivery systems based on hybrid bio-nano-composites with improved magnetic performance of the nanoparticles and maximized therapeutic potential of the drug eluting/retrieval stents by the loaded antioxidative biomolecules layered on the stent surface. In addition, the design of the nanoparticles will include the improvement of the monodispersity, colloidal stability and functionality. Also, further engineering of these nanoparticles and of their formulation as hybrid systems for target delivery will allow improving their bioselectivity and bioefficiency.

Concept and objectives:

- The project with multi-disciplinary character is focused on analysis and solving from the physical, chemical and biochemical viewpoint the design and technology for the stents achievement with drug delivery possibilities, based on antioxidants-loaded core-shell magnetic nanocomposites deposited onto the **stent surface**.
- The market for stents is, in many ways, still emerging. While coronary stents have been on the commercial market in one form or another for several years, the technologies and materials used to create the devices are improving every day. In addition, innovative technology is bringing new classes of devices (e.g., fully degradable stents) to market, technologies that grow the market and even expand means of diagnosis and therapy stent to new patient populations in some cases.
- One of the most innovative aspects of this proposal is the use of functionalized magnetic nanoparticles with antioxidative biomolecules deposited onto the stent surface to realize stent devices type for bio-requirements. Thus the new stent device will function as a delivery platform. At the same time, the prepared MNPs will represent a particularly appropriate tool based on their ability to be simultaneously functionalized and guided and/or removed by an external magnetic field owing to the magnetic NPs inclusion, meanwhile the presence of the antioxidative biomolecules would be the additional benefit. As it is well known stents are scaffoldings, usually cylindrical or tubular in shape, which function to physically hold open and, if desired, to expand the wall of the vessel. Typically stents are capable of being compressed, so that they may be inserted through small cavities via catheters, and then expanded to a larger diameter once they are at the desired location. Although stents are significant innovations in the treatment of occluded vessels, there remains a need for administering therapeutic substances to the treatment site. Systemic administration of the therapeutic substance often produces adverse or toxic side effects for the patient. Local delivery of therapeutic substances, by contrast, provides a smaller overall dosage that is concentrated at a specific treatment site. Local delivery can produce fewer side effects and achieve more effective results. In this context novel formulation based on biocompatible polymers will be developed and applied to create a family of antioxidant magnetic nanoparticles (MNPs) for covering the stent surfaces further characterized as a platform for magnetically guided and delivery of therapeutics. The selected polymers will undergo physical (forming of interpolymer complexes by physical interactions) and chemical (functionalization, derivatization, crosslinking, reactive mixing) modifications in order to obtain stable multifunctional nanosystems. The key features of the new target delivery systems will be investigated, including *in vitro* bioactive compounds activity, capacity to protect the antioxidants from proteolysis, as well as the capacity of the magnetic guidance, retrieval and remove. The project includes aspects like toxicology, biocompatibility of the nanodevices, and also efficacy and biodistribution of the system. In addition, the design of the nanoparticles will include the improvement of the monodispersity, colloidal stability and functionality. Also, further engineering of these nanoparticles and of their formulation as hybrid systems for target delivery will allow improving their bioselectivity and bioefficiency.

Stage I – the obtained results

- In accordance with the plan of the project "Interdisciplinary research on multi-functional hybrid particles for bio-requirements", the stage I/2012 has the objectives:
- (I) **magnetic composites preparation** and (II) their **physical – chemical evaluation**, which were fulfilled by specific activities : - the obtaining of magnetic nanoparticles (NPs) with linking capacity and antioxidant enzymes transport; - the surface modification of magnetic NPs with polymeric structures, as basis for antioxidant hybrid materials; - the characterization of the magnetic composites with the aim of association with antioxidant enzymes and the estimation of the physical-chemical theoretical and experimental conditions necessary for their realization, and the dissemination of the results by national and international symposia communications, publications in the ISI quoted journals or indexed in international databases.
- The conducted studies have resulted in:
- (I) Synthesis and characterization of polymeric matrices, respectively: (1) poly(2-hidroxyethyl methacrilate-co-3,9-divinyl-2,4,8,10-tetra-oxaspiro[5.5]undecan-co-glicidil methacrylate) ternar copolymer (synthesized by radical copolymerization in aqueous dispersion); (2) poly(dimethyl acrylamide-co-3,9-divinyl-2,4,8,10-tetraoxaspiro [5.5]undecan-co-itaconic acid) ternar copolymer (synthesized by radical copolymerization in dimethyl acetamide solution); (3) poly(2-hydroxyethyl methacylate-co-3,9-divinyl-2,4,8,10-tetraoxaspiro [5.5]undecan -co-acrylamide) (synthesized by radical copolymerization in dimethyl acetamide solution); (4) 6 variants of bloc copolymers based on poly(succinimide)-b-poly(ethylene glycol)(PEG) (synthesized by copolycondensation in dimethyl formamide in the presence of Mn(CH3COO)2.2H2O as catalyst), PEG having different molecular weights, such as : 2000, 3000, 4000, 10000, 20000 and 35000; (5) one grafted polymeric structure based on carboxymethyl starch-g-poly(lactic acid);
- (II) The preparation of hybrid structures with magnetic characteristics by using the realized polymeric matrices;
- (III) Testing activities of the polymeric matrices and hybrid structures for coupling of the antioxidant enzymes, in course.
- In the context of the dissemination activity of the results by communications at national and international symposia, by publications in the ISI quoted journals or indexed in international databases, there were presented:
- (a) Three communications at 5th International Conference “Biomaterials. Tissue Engineering and Medical Devices” *BiomMedD’2012*, Constanta, 29 August – 1 September 2012, respectively:
- - Streptavidin-Biofunctionalized Magnetic Particles for Blood Contacting Applications; V. Bălan, M.I. Popa, A.P. Chiriac, I. Neamtu, L.E. Nita, M.T. Nistor, M. Butnaru, L. Verestiuc
- - Bioactive Hybrid Scaffolds in Regenerative Medicine and Tissue Engineering; M.T. Nistor, C. Zgardan, C. Vasile, L.E. Nita, A. Chiriac
- - Assembly Design and Characterization of an Innovative Modulated Drug Delivery System; L. Nita, M. Nistor, N. Tudorachi, I. Neamtu, A. Chiriac
- (b) One communication „Determination of the kinetic parameters and analysis of gases released by thermal decomposition of CMS-g-PLA copolymer” at XXXII National Chemical Conference Rm Valcea, October 2012, and
- (c) One paper accepted for publication in Industrial & Engineering Chemistry Research (IF = 2.237): “Thermal degradation of carboxymethyl starch-g-poly(lactic acid) copolymer by TG-FTIR-MS analysis”, authors Nita Tudorachi, Rodica Lipsa, Fanica Mustata.