

SEVENTH FRAMEWORK PROGRAMME OF THE EUROPEAN UNION
THE PEOPLE PROGRAMME
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Full Title: Nanostructured Biocompatible/Bioactive Materials
Acronym: NANOBIOMAT

Mid-term Report for 2014-2015

PUBLISHABLE SUMMARY

The aim of the Project is to design, develop, fabricate and characterize novel nanostructured bioactive materials (NSBM) for biomedical applications. The Project concept is to bring together research groups specialized in material science and experts in bio-active materials and their application in medicine. Project concept is based on combination of fundamental researches (studying interfacial phenomena and the structure-property relationships) and applied problems in the development of new bionanomaterials. The objectives of the project were based on the principle of interdisciplinary research. The main research objectives of the 4-year joint programme are: to elaborate novel drug-delivery systems based on nanoporous or nanoparticulate oxides, synthetic polymers and biopolymers; to synthesize and characterize NSBM with immobilised metal and metal oxide nanoparticles with bactericidal properties; to expand the modification of NSBM to improve their biocompatibility, to develop porous polymeric monoliths and disperse materials for pollutant and biotoxins removal from liquid media under static and dynamic regimes; to develop new NSBM based on semi-interpenetrating polymer networks (IPN) filled with metal, oxide and carbon nanoparticles for medical applications and optimize their physicochemical and mechanical properties; to elucidate the mechanisms of adsorption of bioactive compounds from aqueous solutions and biological media on NSBM; to study the structure-property relationships and a role of interfacial phenomena in performance of NSBM.

The progress and achievements of the work performed in 2014-2015:

WP1 Drug delivery systems based on nanoporous or nanoparticulate oxides and polymers

- Synthesis and investigation of biopolymer nanogels based on modified tannins for obtaining biomedical films with enhanced therapeutic activities and suitable for encapsulation of low molecular biomolecules.
- Synthesis and investigation of nonporous and porous silicas with attached chitosan, aminopropyl radicals, nitrogen-contained polymers, guanidine, polydimethyl- or polymethylphenylsiloxanes with different structure of surface layer.

- Method for encapsulation of bioobjects by hydrophobic silica.
- Synthesis and investigation of: silica carriers encapsulated into chitosan, stable dispersion of nanodiamonds, suspensions of microorganisms encapsulated by hydrophobic silica, polymeric films based on sol-gel filled chitosan or polyhydroxyethylmethacrylate, films filled with pristine and modified carbon nanotubes.
- Characterization of structure and sorption activity of NSMs with adsorbed polydimethylsiloxane.
- Synthesis and investigation of the magneto-sensitive nanoparticles, silica based mixed oxides and thermostable hybrid materials.
- Synthesis and surface functionalization of chitosan-mineral carriers.
- Synthesis of the biocompatible hydroxyapatite/carbon nanotubes composites.

WP2 NO-releasing nanostructured surfaces

- Method for coating of stainless steel substrate with TiO.
- An *Ex-vivo* method for NO measurement based on vascular studies alternative to the conventional Griess method.
- Elaborating stainless steel and silica modified with NO-releasing compounds (native and iron-sulfur cluster nitrosyl complex) or cerium oxide nanoparticles.
- The polymeric films based on filled chitosan, HEMA, polystyrene for stents coatings were developed.
- Synthesis of polymeric films filled (and unfilled) with nanoparticles with and without nitrosylated biomolecules (S-nitroso-glutathione and S-nitrosoalbumin), and polymeric films based on polyHEMA and CNTs with low swelling degree and smooth surface.

WP3 Biocompatible homopolymeric and IPN-based nanocomposites filled with oxide, carbon or metal nanoparticles and biocompatibility improving additives

- Investigation of thermal transitions and molecular dynamics in chitosan/nanosilica systems, hybrid materials based on modified silicas and poly(dimethylsiloxane) (PDMS), nanocomposites based on nanosized silica with adsorbed or chemisorbed carbonaceous precursor by various techniques.
- Investigation of thermal transitions, segmental dynamics and hydration properties of silica/PMS and silica/PMPS nanocomposites, as well as of CNT filled films based on polystyrene, chitosan and polyHEMA.
- Studies of structure and dynamics of nanocomposites based on polyurethane-poly(2-hydroxyethyl methacrylate) semi-interpenetrating polymer networks and aminoacid-modified nanosilica.
- Functionalised NPs of silica, metal oxides or metal NPs and nanocarbons with required surface characteristics were obtained.
- Study of a structure and morphology of nanofillers and their interfacial interactions with modifying reagents.
- Synthesis of nanocomposites based on poly(hydroxyethyl methacrylate); poly(vinyl alcohol) (PVA), poly(ethylene glycol) (PEG), gelatine, chitosan, polystyrene doped with oxide (silica, magnetite and other metal oxides), carbon (nanotubes, graphite) or metal NPs.
- Magnetic field-ordered polymeric composites based on chitosan, HEMA or styrene filled with modified carbon nanotubes obtained and characterized.

- The homopolymeric films with interpenetrated silica network with different internal structure and swelling properties synthesised and studied.
- The effect of filler and crosslinker nature and functionality on internal structure and polymeric chain mobility studied using polymeric chitosan films.
- Experimental studies of properties of organic-inorganic films based on biopolymer chitosan and silica and organosilica with amino groups synthesised using sol-gel transformations and application of bifunctional cross-linking reagents performed.
- The syntheses of novel cryogel materials based on acrylamide cross-linked with ZrO₂ nanoparticles performed.

WP4 Nanostructured materials with immobilised bactericides

- Synthesis of Enoxil, product obtained by modification of grape seeds tannins.
- Synthesis of polyfunctionalised nanocomposites (silica) with bactericide compounds (Enoxil); development of new approaches to obtain complex silica/Enoxil nanomaterials with enhanced antibacterial properties.
- Development of a method for preparing of tannin/polyvinylpyrrolidone nanocomposite films and Investigation of their antimicrobial activity.
- Modification of zirconia nanoparticles surface by hydroxyethyl methacrylate (HEMA). Synthesis of porous hybrid cryogels based on polyacrylamides and ZrO₂-Tb₂O₃ nanoparticles by radical polymerization.
- Elaborating new approaches to synthesise nanocomposites with bactericide; synthesis of polyfunctionalised silica and carbon materials with immobilised metal NPs (Cu, Ag, Se), chlorhexidine or polyphenols.
- Synthesis of polymeric films filled (and unfilled) with nanoparticles with and without bacteriostatic agents.
- Synthesis of the composites based on chitosan or HEMA with chlorhexidine (EnoXil, ALDIM) unfilled and filled with modified carbon nanotubes, colloidal graphite or sol-gel silica
- Synthesis and characterization of carbon composites containing Fe, Co, Ni nanoparticles.
- An effective method of producing hybrid bactericidal material based on nanosized Ag and Ag/Cu composite.
- Enhancement of antioxidant and antibacterial activities by immobilization of natural bactericide into hybrid supramolecular chitosan biocomposite gel.
- The immobilization of modified natural polyphenol bactericide into hybrid supra-molecular chitosan bio-composite gel with enhanced antioxidant and antibacterial properties (e.g. antioxidant activity) for biomedical applications.
- A novel bio-composite material with enhanced bacteriostatic action against *S.aureus*, *E.coli* and *B.cereus* bacteria pathogens frequently identified in open trauma skin infections.
- A number of composite films based on biocompatible, biodegradable and non-toxic biopolymer chitosan containing natural polyphenol bactericide (Enoxil) for biomedical applications of materials with enhanced antioxidant and antibacterial properties.
- Novel chitosan-based bio-composite films with natural bactericide Enoxil and hydroxyethyl cellulose (HEC) synthesised.

WP5 Porous polymeric and carbon adsorbents for removal of pollutants and biotoxins

- The procedure to produce carbon monoliths and nanoporous carbon adsorbents with controlled structure via carbonisation of different type of precursors developed.
- Several types of carbon porous materials with different textural and adsorption characteristics obtained.
- The titania-coated nanosilica-cobalt ferrite composites for photocatalytic removal of pollutants from water synthesised.
- Magnetosensitive Ni/C nanocomposites with porous shell synthesised and characterised.
- Interfacial phenomena at various interfaces studied.
- Synthesis of polyfunctionalised carbon materials with immobilized bactericide nanoparticles (Ag, Se).
- Effects of adsorbent surface and structure properties on equilibrium and kinetics of selected pollutants studied.

WP6 Adsorption of bio-active compounds on hydrophilic and hydrophobic surfaces

- Preparation of systems based on nanosilica and chitosan by various methods.
- Study of structure-adsorptive properties of silicas and carbon materials.
- Studies of interfacial phenomena in various silica, nanosilica, metal-oxide and polymeric systems and composites
- New sorbents based on silica and saponite with immobilised chitosan elaborated and tested in extraction of V(V), Mo(VI) and Cr(VI) oxoanions.
- New sorbents based on hydroxyapatite and nanotubes obtained.
- The investigation by various techniques of a mechanism and kinetics of the reaction of siloxanes' depolymerisation in the presence of dimethyl carbonate.
- Adsorption, electrokinetic and stabilizing properties of the system: guar gum/surfactant/alumina.
- Investigation of the polyvinyl alcohol stabilization mechanism and adsorption properties on the surface of ternary mixed nanooxide $\text{Al}_2\text{O}_3\text{-SiO}_2\text{-TiO}_2$.
- The adsorption of polysaccharides (agar, pectins with high and low degree of esterification, sodium alginate, chitosan) and polyols (maltitol, isomaltitol, erythritol) on silica studied.
- A set of mathematical models for characterisation of structural and textural characteristics of different materials developed in collaboration of PABS, Brighton University and CISC team (ISC, Kyiv).
- Measurements and analysis of adsorption equilibrium and kinetics for proteins, pharmaceuticals and other bioactive compounds on siliceous and carbonaceous materials.

WP7 Structure-property relationships and the role of interfacial phenomena in performance of nanostructured biomaterials

- Investigation of thermal transitions, segmental dynamics and hydration properties of polymer nanocomposites based on semi-IPNS PU-PHEMA and silica modified with triptophane.

- The structure of chemically immobilized polysiloxanes (PDMS, PMPS) on silica, titania or mixed oxides was studied and structure-property relationships was elucidated.
- Characterization of polymer nanocomposites based on semi-interpenetrating polymer networks of PU and PHEMA as matrix and carbon nanotubes (CNTs) as filler and investigation of their structure-properties relationships by a variety of experimental techniques.
- A model based on different conformations of polymers adsorbed on nanooxides developed and applied for the interpretation of experimental results.

Proposed in the Project the mobility exchange scheme, training and innovation potential strengthen the scientific cooperation between the EU and Eastern European Countries. An extensive cooperation of researchers from these countries will results in a large number of achievements: syntheses of advanced materials with great potential to be used in medical applications, exchange of ideas, joint publications, patents and more effective use of scientific equipment.