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Posters

Patricia Gálvez-Martín et al., J Biotechnol Biomater 2017, 7:2 (Suppl)
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Development of scaffolds for regenerative medicine

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Statement of the Problem: Regenerative medicine refers to methods to regenerate or replace human cells, tissues or organs in order to restore or establish normal function. The clinical use of stem cells, genes and tissues constitutes a new range of advanced therapy medicinal products (ATMPs) such as gene therapy medicinal products, somatic cell therapy medicinal products, tissue engineered products and combined advanced therapies' products. Each of them can be formulated with different types of biomaterials to provide greater cell viability, such as release systems, scaffolds, etc. The purpose of this study is to describe the different products with stem cells and scaffolds that should be considered ATMPs for clinical application, to classify the different types of medicinal products and meet the legal requirements for their marketing authorisation.

Methodology & Theoretical Orientation: The aim of this study was to define the main biomaterials used in ATMPs and medical devices, and the regulatory aspects for their clinical application. Thus, we searched the main available databases up to September 2016.

Findings: Major advances in advanced therapies focus on the development of matrices made of natural or synthetic origin biomaterials such as collagen, alginate, hyaluronic acid, polyethylene glycol, etc. All of them should be considered medical devices by themselves, but if each scaffold is combined with stem cells, tissues or genes, they will be considered medicinal products.

Conclusion & Significance: The ability to combine cells, tissues and genes with biomaterial manufactured structures to develop medicinal products, opens up new prospects in the administration of these ATMPs in the area of regenerative medicine.

Biography

Patricia Galvez-Martin, completed her PhD in 2014, MSc in Drug Development (2008) and MSc in Clinical Trials (2012). She has participated in several clinical trials, with great experience in the pharmaceutical industry, as Qualified Person and Quality Control Manager. She is expert in the design and development of new medicines with cells, genes and tissues to treat different pathologies. She is currently working in the biotech company Bioibérica as the Director of the Advanced Therapies Unit.

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Novel extended-released polymeric matrix for Monascus fermented rice extract (RYR) delivery

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Monascus fermented red rice (RYR) has been demonstrated to lower cholesterol in blood and sold over-the-counter as an alternative to cholesterol-lowering statin drugs, especially for who stopped statin drugs due to their side effects. The goal of this work is to develop an extended-release formulation, able to maintain the activity effect against the cholesterol, obtaining a constant release of statins present in RYR throughout the staying of the tablets inside the intestine. This study focus on the analysis of different carriers for controlled release systems composed by polysaccharide-based matrices by two different formulations based on K-Carrageenan and Gellan gum (ranging from 10-90% in weight). Samples as cylindrical tablets have been physicochemical characterized by FTIR, DSC, TGA, Rheometer and TOF-SIMS, water uptake, water bond, water diffusion and mesoporosity. The Monacolin K release has been monitored until 48 hours in simulated intestinal fluid SIF. HMG-CoA reductase activity has been measured to determine the formulation influence on statin activities against the Lovastatin activity used as control. The selected formulation enhances the statins release respect to the RYR matrix alone and in addition, the preliminary biological results suggest that the activity of these samples is associated with the inhibition of HMG-CoA reductase. Release tests pointed out that formulations obtained combining polymers in a ratio close to 1 (i.e., 40/60 and 50/50) guaranteed a potentiated release of Lovastatin from RYR inducing also a superior hypocholesterolemizing action both in terms of hepatocytes cholesterol production and inhibitory activity towards 3-hydroxy-3-methylglutaryl-coenzyme A reductase (HMG-CoA). The most effective one, in hypocholesterolemizing activity, in terms of inhibitory activity versus HMG-CoA reductase and hepatocytes cholesterol production, was the formulation obtained combining 40% of K-Carrageenan and 60% of Gellan gum.

Biography

Marco Consumi is a Research Scientist at Department of Biotechnology, Chemistry and Pharmacy in University of Siena, Italy. He has received his PhD in Biomaterials from University of Trento and studied polymers and polymer based materials for controlled release of active substances in pharmaceutical and nutraceutical field. As a Postdoctoral Fellow, he was focused on understanding the correlation between the chemical composition of materials and their biological activity. He has broad expertise in synthesis modification and characterization of polymers (naturals and synthetics) and materials for biomedical applications. Actually, he is involved in 2 EU ITN projects in bacterial infection topic to fundamentally better understand the biology, chemistry and physical properties of biofilms and 2 Toscany Region funded projects on nutraceutical filed.

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Wear particle embedded 3D agarose gels for biocompatibility testing of orthopedic medical devices

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Background: We have developed a single method using 3D agarose gels that is suitable to test the biocompatibility of all three types of wear debris (Polyethylene, Ceramic and Metal) simultaneously.

Methodology & Theoretical Orientation: Clinically relevant sterile UHMWPE and CoCr wear particles were generated using methodologies described previously. Commercially available nanoscale and micron-sized silicon nitride (SiN) particles (<50 nm and <1 μm, Sigma UK) were sterilized by heat treatment for 4 hours at 180 °C. Agarose-particle suspensions were prepared by mixing warm 2% (w/v) low-melting-point agarose solution with the particles dispersed by sonication in DMEM culture media. The suspensions were then allowed to set at room temperature for 10 min in 96 well culture plates. Sub-confluent L929 murine fibroblasts were cultured on the prepared gels for up to 6 days in 5% (v/v) CO_2 at 37 °C. After incubation, the viability of cells was measured using the ATP-lite assay; the results were expressed as mean±95% confidence limits and the data was analyzed using one-way ANOVA and Tukey-Kramer post-hoc analysis.

Findings: The gels were observed to ensure uniform distribution of particles and migration of cells into the gel. No significant reductions in viability were observed for nanoscale and microscale SiN particles at low doses (0.5 μm^3 per cell) and high doses (50 μm per cell) or for UHMWPE wear debris at high doses (100 μm^3 per cell). Moreover, the viability was significantly reduced for high doses of CoCr wear debris (50 μm^3 per cell) and the positive control, Camptothecin (2 $\mu g.ml^{-1}$) at day 6. These results are consistent with the literature and therefore validate our 3D agarose cell culture method.

Conclusion & Significance: Biocompatibility of polymer, metal and ceramic wear debris can be tested simultaneously by using 3D particle embedded agarose gels.

Biography

Richard M Hall is a Member of the University of Leeds with an interest in motion preservation devices as well as research in to spinal cord injury and augmentation procedures such as vertebroplasty. He currently coordinates the LifeLongJoints project and is the Director of Postgraduate Research Studies in Engineering.

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Dissolving microneedles: An attractive approach to transdermal drug delivery

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The microneedle-mediated transdermal delivery system has been developed to provide minimal invasive self-administration method with patient friendly manner. Especially, dissolving microneedles, which deliver the target drugs as the drug-loaded microneedle dissolves into the skin, have been spotlighted recently. Droplet-born air blowing (DAB) fabrication method has advantages in stability with precise dose control because DAB provides quick manufacturing process with ambient temperature. The purpose of this study is to show the characteristics of dissolving microneedles, which were manufactured in our mass production system. Microneedle was fabricated by DAB method. The loaded amount of vitamin C and vitamin B3 was analyzed by HPLC/UV system was used to assay the loaded amount within microneedles; and delivered amount of drug into the skin was analyzed using Franz diffusion cell (Logan, FDC-6T). We optimized the DAB process parameters and scaled up. 350 μm and 500 μm length of HA microneedles were fabricated and dried within 10 min without applying any heat. The stability of EGF within HA microneedle was investigated during 2 months at 25, 45°C and was confirmed. The anti-oxidant was stable within HA microneedle during 2 months at 25°C and 45°C. *In vitro* and ex vivo studies using Franz diffusion cell showed excellent delivery efficiency compared to topical solution. Most of the loaded anti-oxidants was delivered through the skin after 24 hr (98.0±2.0%, n=3). The microneedles dissolution in skin was confirmed, so the drugs within microneedle should be delivered into the intradermal region. Based on the method, we loaded lots of active ingredients with precise dose control, and confirmed the stability of labile drugs such as peptide drugs and anti-oxidants within microneedles. We are investigating the formulations for biopharmaceutics using this platform technology.

Biography

Na Keum Jang received her BS degree in Animal Biotechnology and MS degree at the Department of BIN Fusion Technology, Chonbuk National University, Republic of Korea. Her research interest includes synthesis of polymeric biomaterials for regenerative medicine and sensors applications. Now she is studying microneedle patch for transdermal drug delivery system at Raphas Co. Ltd.

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Novel resorbable and osteoconductive nurse'A phase-silicocarnotite scaffold induced bone formation

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Alternatives to natural bone grafts are needed in a society that progressively prolonged life expectancy, and it should address the health problems of an aging population. In this context calcium silicophosphate scaffolds are promising candidates. Composition belongs to subsystem Nurse's A-phase-Silicocarnotite was selected for the ceramic scaffolds that were prepared by the polymer replication method. An interconnected porous structure with a striking similarity to human cancellous bone tissue was obtained. Response to ceramic scaffolds was evaluated by implantation in New Zealand tibia rabbits in periods of 3 and 6 months. Radiological studies showed correct integration and partial resorption of the scaffold. Histological results presented no evidence for inflammation or infection at the implantation sites. Colonization process of the scaffold started in the periphery and then penetrated throughout implant porosity. Scaffolds degraded over time and that degradation happened according to the tissue in-growth rate. Histomorphometric analysis gave high BIC values (67.30% ± 1.41) opposite to control samples, where newly formed bone in the cortical defect increased in a smaller amount than in the grafted defects. After six months of implantation SEM studies reveal that the whole ceramic implant surface was covered by a newly formed bone tissue. The new bone layer was composed of Ca-P, mainly with traces of Si due to the gradual diffusion of Si ions from the scaffolds into the newly forming bone, which formed part of the biomaterial's resorption process. The results indicate that this material provides an optimal microenvironment for the osteogenic differentiation of the undifferentiated osteoblastic precursor cells contained in hematopoietic bone marrow.

Biography

Patricia Mazón studied Chemistry at the University of Alicante, and pursued her PhD about aminoacids synthesis. She started her adventure in Biomaterials field in 2012 at the University Miguel Hernández. Currently, she is a Professor at the Department of Materials Science, Optic and Electronic Technology and Researcher at the Biomaterials area of Bioengineering Institute.

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Evaluation of anti-biofilm properties of titanium nitride coatings: An *in vitro* study

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Statement of the Problem: Biomaterial associated infections are challenging to treat due to bacterial biofilm formation. Infections around dental implants (so called peri-implantitis) may occur both shortly after implantation as well as after several years. Some risk factors are patient related, such as a prior history of periodontitis, poor oral hygiene, and smoking. However, product properties have also been indicated to influence the risk, progression, and resolution of peri-implantitis. It is hypothesized that anti-biofilm surface modifications may have a counteracting effect in the progress of infection and thereby reducing the risk of infection. Titanium nitride (TiN) coatings are used for dental abutments due to its golden color, but have also been found to accumulate less amounts of plaque. However, there is limited knowledge on possible mode of action. The purpose of this study is to characterize the surface properties of TiN and to investigate biofilm formation on TiN in comparison with Ti.

Methodology: Pre-conditioned specimens were incubated with a co-culture of different oral bacterial species for up to four days. Biofilm formation was evaluated with plate counts, qPCR, live/dead, and crystal violet. Ti and TiN specimens were also characterized using a set of different surface analytical techniques.

Findings: After 24 h, plate counts showed a log 2 reduction of bacterial load on TiN compared to Ti, while qPCR failed to show a difference. Live/dead indicated that the biofilm is thinner on TiN than on Ti.

Conclusion & Significance: TiN was found to have a certain degree of anti-biofilm properties *in vitro*. However, any conclusions on clinical significance need data from randomized clinical studies.

Biography

Anna Arvidsson has her expertise in biomaterials and medical device surfaces, with a specific interest related to infection. She has an interdisciplinary background within engineering biology, directed towards biomaterials. During years at Göteborg University with research on surface mediated interactions at the bone/soft tissue implant interface, she has gained experience in surface modifications, surface characterization, and *in vitro* and *in vivo* models. Based on this knowledge, she is now creating and exploring new innovations at Dentsply Sirona Implants with purpose to further improve dental implant treatments and tissue regeneration.

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Isolation of low volumes of silicon nitride particles from tissue

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Adverse biological responses to wear debris generated by total hip replacements (THRs) limit the lifetime of such devices. This has led to the development of biocompatible coatings for prostheses. Silicon nitride (SiN) coatings are highly wear resistant and any resultant wear debris is soluble, reducing the possibility of a chronic inflammatory reaction. SiN wear debris produced from coatings has not been characterized *in vivo*. The aim of this research is to develop a sensitive method for isolating low volumes of SiN wear debris from periprosthetic tissue. Commercial silicon nitride particles of <50 nm (Sigma Aldrich) were incubated with formalin fixed sheep synovium at a volume of 0.01 mm3/g of tissue (n=3). The tissue was digested with papain (1.56 mg/ml) and proteinase K (1 mg/ml) and samples were subjected to density gradient ultracentrifugation using sodium polytungstate (SPT) to remove protein from the particles. Control tissue samples, to which no particles were added, were also subjected to the procedure. Particles were washed to remove residual SPT and filtered onto 15 nm filters. The filtered particles were imaged by scanning electron microscopy and positively identified by elemental analysis before and after the isolation procedure. To validate whether the isolation method affected particle size or morphology, imaging software (imageJ) was used to determine size distributions and morphological parameters of the particles. A Kolmogorov-Smirnov test was used to statistically analyze the data. The particle size distributions of isolated and non-isolated particles were similar. Morphology in terms of roundness and aspect ratio was unchanged by the procedure. Future work aims to test the method on titanium and cobalt chrome wear debris generated by a pin-on-plate wear simulator. The method will then be applied to isolate and characterize particles from *in vivo* studies of novel SiN coated prostheses in a rabbit and sheep model.

Biography

Richard M Hall is a Member of the University of Leeds with an interest in motion preservation devices as well as research in to spinal cord injury and augmentation procedures such as vertebroplasty. He currently coordinates the LifeLongJoints project and is the Director of Postgraduate Research Studies in Engineering.

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Multi-walled carbon nanotubes (MWCNTs) as cytotoxic drug delivery systems in the treatment of cancer

Eloisa Gonzalez-Lavado[1], **Esperanza Padin-Gonzalez**[1], **Nerea Iturrioz**[1], **Tomas Torroba**[2] and **Monica L Fanarraga**[1]
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Our laboratory has focused on the intrinsic anti-proliferative, anti- migratory and cytotoxic effects of carbon nanotubes (CNTs). We have shown how MWCNTs interact with microtubules assembling biosynthetic polymers triggering serious biomechanical cellular defects that lead to cancer cell death. These properties of CNTs produce antitumoral effects in solid melanoma tumors *in vivo*. The huge surface area of CNTs maximizes their ability to interact with many biological components and different chemicals, constituting their biocorona. Taking into account these surface properties, we aimed to increase these intrinsic antitumoral effects of CNTs functionalizing these nanomaterials with a well-known anti-tumoral drug (5-fluoracil) *in vitro* in melanoma cells and *in vivo* in solid malignant melanomas produced by allograft transplantation in murine recipients. We have double-coated CNTs with an internal chemical layer surrounded by a second coat of proteins. The first layer carrying chemicals, either a dye (as a proof-of-concept) or a drug (5-fluoracil) and the second being a serum protein coating layer, both assembling the biocorona. The protein coating serves for (1) CNTs recognition by cellular receptors, (2) endocytosis, (3) protection of the chemical component attached to the nanotube surface until protein degradation that takes place at the lysosome, and (4) the release of the transported drug during the first 5-9 hours next to the internalization process. CNTs loaded with 5-fluoracil double coated with serum proteins display a significantly enhanced antitumoral effect *in vitro* and *in vivo* in mice bearing solid melanoma tumors.

Biography

Eloisa Gonzalez-Lavado is a PhD student in the Nanomedicine Group of the University of Cantabria (Spain). I did a chemistry Bachelor's degree at the University of Extremadura (Spain).I have an european interuniversity master's degree in theoretical chemistry and computational modelling. Currently I am working with carbon nanotubes and their biomedical aplications, especially in Cancer, studying their biocompatibility, their capability as nanocarriers and their own antitumoral effect.

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Nanogels preparation for controlled bioactives' delivery

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Petru Poni Institute of Macromolecular Chemistry, Romania

Nanogels are cross-linked polymeric particles, which can be considered as hydrogels if they are composed of water soluble/swellable polymer chains. Their applications for polymer-based bioactives' delivery systems require biodegradability, controlled particle size with uniform diameter, large surface areas for multivalent bioconjugation and interior network for the incorporation of different therapeutics, environmental-stimuli responsive capability, dispersibility in biological fluids, sustained release in time of bioactives and facile removal of the devices after the bioactives delivery, etc. This study describes the synthesis and characterization of a stimuli-responsive nanogel performed by crosslinking poly(itaconic anhydride-co-3,9-divinyl-2,4,8,10-tetraoxaspiro [5.5] undecane) with 1,12 dodecandiol. The copolymer with different ratios between the two comonomers is able for network formation, binding properties, amphilicity, and good oxidative and thermal stability. At the same time the new nanogel structure has high functionality, biocompatibility, temperature and pH responsivity, and is designed to have potential biomedical applications. The chemical structure is explored utilizing common spectroscopic analyses, while the dual pH and temperature sensitivity is evaluated by determining the hydrodynamic radius and zeta potential by dynamic light scattering technique. The analysis of the thermal stability by thermogravimetric analysis supports the new covalent bonds realized by the crosslinking reaction between the copolymer and diol. The acute toxicity of the nanogel is estimated after mice oral administration. Accordingly, analysis of histological evaluation of liver tissues does not reveal substantial pathological modifications. The results propose that the nanogel may be suitable for *in vivo* use as bioactives' delivery system.

Biography

Iordana Neamtu is a Senior Scientific Researcher at "Petru Poni" Institute of Macromolecular Chemistry in Iasi - Romania. Her expertise is in synthesis of polymer materials with potential biomedical applications. She has published more than 50 papers in reputed journals and participated in more than 15 Romanian Projects.

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Co-immobilization of glucose oxidase and catalase on electrodes' surface: A multifunctional tool for biosensing applications

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Real world application of reductase-based electrochemical biosensing devices is limited by the need of anaerobic working conditions. Molecular oxygen is a main interferent because (a) it can react with many redox mediators in their reduced form, and (b) the reduction of oxygen at the working electrode surface generates an intense background noise that can mask important redox processes occurring between -200 and -800 mV (vs SHE). Standard laboratorial oxygen removal strategies, such as argon purging or vacuum degassing, are incompatible with on-site monitoring. Alternatively, a bi-enzymatic scavenging system that efficiently reduces the soluble oxygen content in small volume samples, and can maintain anaerobic conditions in an open-air environment for extended periods of time, was adapted for biosensing purposes. The scavenging system is composed by glucose oxidase (GOx) and catalase (Cat) in solution and uses the glucose as main substrate, removing oxygen in a two-step cycle. This strategy was successfully employed with a miniaturized reductase-based biosensing tool to monitor nitrite in real samples. We now aim at making the scavenging system an integral part of the biosensors, simplifying operating procedures and reducing costs. Therefore, we have immobilized GOx and Cat on pyrolytic graphite electrodes, using a silica sol-gel matrix, and tested the system's ability to provide local anaerobic conditions. Several combinations of GOx/Cat in solution and in the immobilized state were prepared and the electrochemical response, in non-deareated solutions containing glucose, was monitored by cyclic voltammetry. Our results showed that although the scavenging system was more effective when in solution, the co-immobilized GOx and Cat were still able to provide a satisfactory anaerobic environment. Additionally, the configurations containing either immobilized GOx or Cat were explored as biosensing tools to monitor glucose and hydrogen peroxide, respectively. The GOx-based bioelectrode responded linearly to glucose concentrations from 1.2 – 7 mM.

Biography

Tiago Monteiro is a second year PhD student at the Doctoral Program in Sustainable Chemistry at Faculdade de Ciências e Tecnlogia, Universidade Nova de Lisboa, Portugal. He has previously obtained a MSc degree in Biotechnology (2013) and a BSc degree in Molecular and Cellular Biology (2011) at the same institution.

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New method for magnetic composite deposition onto a stent surface

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Petru Poni Institute of Macromolecular Chemistry, Romania

The study is devoted to investigating the possibility of using an alternating magnetic field (AMF) for deposition and covering a stent surface and improve its functionalities with a new magnetic composite (MC). MC was prepared *in situ* during functionalization of poly(maleic anhydride-co-3,9-divinyl-2,4,8,10-tetraoxaspiro [5.5] undecane) copolymer by opening the anhydride ring with erythritol and introducing magnetic nanoparticles into the polymer matrix. Ten different solvents were used to evidence the dependence between AMF presence, the reaction medium characteristics and the kinetic deposition. Interdependence among the viscosity, density and molar polarization of the solvents and the yield of deposition was registered. The covering of stent with MC is also analyzed by microscopy and the new magnetization values are estimated.

Biography

Aurica P Chiriac has completed her PhD in 1994. She has published more than 100 papers in reputed journals and is an Editorial Board Member of some reputed journals. She participated in more than 15 Romanian Projects and 5 European Projects.

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Production and characterization of bioceramic nanopowders of biological origin

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The regeneration potential of human bone to repair large bone defects often requires biomaterials, such as those associated with comminuted fractures or bone tumor resection. The need for bone substitutes is rapidly increasing and many researches have been done to improve their performance. Calcium phosphate based bioceramics have been used due to their high bio-compatibility and their successful use of orthopedic and dental applications. Calcium phosphate bioceramics are similar to bone and tooth minerals due to their chemical and crystallographic properties; hence it is particular interest for bone grafting, augmentation in maxillofacial surgery and in orthopedics as a filling material. Many marine structures are composed of calcium carbonate (aragonite or calcite) and can be converted to calcium phosphate materials by chemical exchange. In this study structural and chemical properties of *Clinocardium ciliatum* based bio ceramic materials (TCP, B-TCP and other phases) were produced by using mechano-chemical (hot-plate) conversion method. At three varying temperature of 450°C, 850°C and 1200°C the materials were transformed to various bioceramic phases. For complete characterization of the bioceramics produced Fourier Transform Infrared Spectroscopy (FTIR), x-ray diffraction (XRD), Brunauer–Emmett–Teller (BET) and differential thermal analysis (TG/DTA) analyses were carried out.

Biography

Zeynep Orman has graduated from Chemical Engineering department and currently studying Bioceramics for her Master's studies in Yildiz Technical University. She is experienced in polymers research and has conducted a project about solar cell studies.

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Nanostructures based on poly(aspartic acid) and bovine albumin by self-assembling procedure

Loredana E Nita, Aurica P Chiriac, Alina Diaconu, Maria Bercea and **Mihai Asandulesa**
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In the last decades, considerable attention has been dedicated to study of interactions between polymer-polymer pair and interpolymer complexes. In this contest, the self-assembling procedure for preparation of functional nanostructure based on linear polyampholyte polypeptide, poly(aspartic acid) (PAS) and a globular protein, bovine serum albumin (BSA), have been studied. The main interest was to identify the formation of an interpenetrated complex between a natural protein and a synthetic polymer in order to design materials suitable for biomedical applications, such as carriers for drug delivery. From the viscometric investigation of PAS/BSA/water ternary systems, it was observed that, for x* value near 0.5, the maximum of intermolecular interactions among the two polymeric partners take place. This statement is sustained by the strong raise of the hydrodynamic radius in the same area of composition. Dielectric spectroscopy data also provide the higher compatibility of PAS with BSA protein molecules and confirm the best conditions for a stable interpolymer complex formation by self-assembling at the PAS/BSA molar ratio x* of 0.542 in aqueous solution. Thus, it is quite important for having desired properties - chemical and biological - the setting and fulfillment of the conditions for achieving the non-covalent forces to make highly functional nanoscale compounds.

Biography

Loredana E Nita is currently a Senior Researcher at Petru Poni Institute of Macromolecular Chemistry, Romania. She has completed her PhD in Chemistry in 2007 at Petru Poni Institute of Macromolecular Chemistry. She has published more than 100 papers in reputed journals and is a member in Editorial Board of some reputed journals. She participated in more than 15 Romanian Projects and 5 European Projects.

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Formation and characterization of biomimetic calcium phosphate coatings on nanostructured surfaces of anodized titanium

Shaghayegh Javadi, Zahra Mohammadi and **A S Mehdi Mesgar**
Tehran University, Iran

Biomimetic coating procedure was used to deposit a bioactive layer of hydroxyapatite (HA) on the surface – modified titanium by anodization process. The anodization was performed on the clean surface of titanium under three different voltages of 80, 100 and 130v using HF as the electrolyte. The morphology, structure and topography of the anodized substrates were evaluated by Scaning Electron Microscopy (SEM) or Field Emission Scanning Electron Microscopy (FE-SEM), X ray Diffraction (XRD) and Atomic Force Microscopy (AFM), respectively. Biomimetic coatings were deposited on the surface of anodized titanium using a two-stage procedure by immersion in two concentrated Simulated Body Fluids (SBF) with different concentration of Mg^{+2} and HCO_3^{-2} ions under physiological conditions. The results showed that an increase in anodization voltage tends to produce a porous surface with circular pores toward a columnar layer of rutile. The surface roughness of anodized surfaces was increased by increasing voltage. Biomimetic coating procedure was caused to form a HA layer which was proved by XRD, FTIR and SEM. The HA layer formed on the anodized titanium surface has a whisker-like morphology. The crystallinity of HA layer was increased by an increase in voltage. The findings indicate that the anodized titanium at high voltages may be suitable substrate for biomimetic coating procedure.

Biography

Shghayageh Javadi did her Master's degree in Biomedical Engineering. Her thesis is about biomaterial coating and focused on best coating method of biomaterials. She has researched on different pretreatment for surface modification of titanium. She has used anodizing process with combination of alkali treatment for surface modification of titanium. The result of her search and experiments showed that the anodized titanium at high voltages may be suitable substrate for biomimetic coating procedure.

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Viscoelasticity of dental polymers used for orthodontic applications

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Aim: To evaluate the viscoelastic properties of two experimental BPA-free and one BisGMA-based orthodontic resin composite adhesives for bonding fixed retainers.

Materials & Methods: A commercially available BisGMA-based (TXA: Transbond LR) and two Bisphenol A-free experimental adhesives (EXA and EXB) were included in the study. The viscoelastic behaviour of the adhesives were evaluated under static and dynamic conditions at dry and wet states and at various temperatures (21, 37, 50°C). The parameters determined were shear modulus (G), Young's modulus (E) under static testing and storage modulus (G1), loss tangent (tan δ) and dynamic viscosity (n*) under dynamic testing. Statistical analysis was performed by 2-way ANOVA and Bonferroni post-hoc tests (α=0.05).

Results: For static testing, a significant difference was found within material and storage condition variables and a significant interaction between the two independent variables ($p<0.001$ for G and E). EXA demonstrated the highest G and E values at 21°C/dry group. Dry specimens showed the highest G and E values, but with no significant difference from 21°C/wet specimens, except EXA in G. Wet storage at higher temperatures (37°C and 50°C) adversely affected all the materials to a degree ranging from 40-60% ($p<0.001$). For dynamic testing, a significant difference was also found in material and testing condition groups, with a significant interaction between the two independent variables ($p<0.001$ for G1 and n*, $p<0.01$ for tan δ). Reduction in G1, and n* values, and increase in tan δ values were encountered at increased water temperatures.

Biography

T Eliades is a Professor and Director of the Clinic of Orthodontic and Paediatric Dentistry, University of Zurich, Switzerland.

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Silkworm gut fibers as novel biomaterials for tissue engineering applications

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Silk fibroin has been largely studied in tissue engineering due to its excellent physical and biological properties. Based on this, we have developed a new biomaterial consisting of high performance fibers produced directly from the silk glands of silkworms (*Bombyxmori*) called silkworm gut fibers. This novel biomaterial could be a potential solution in tendon and ligament repair, as these are very common injuries and the traditional surgical reconstruction including auto/allograft and ligament prostheses implants can involve several complications. With this aim, we have braided the silkworm gut fibers, in order to explore the possibility to create a consistent scaffold for ligament repair. The production of the silkworm gut fibers is based on a traditional procedure that consists of immersion of the silk glands in an acidic solution and a subsequent stretching. We evaluated the mechanical properties of 3 silkworm gut fibers weaved in three-strand braids. The biocompatibility assay was also performed by seeding bone marrow adult human mesenchymal stem cells (*ah*MSCs) on the braided material. 7, 14 and 21 days after seeding, adhesion and proliferation, the cells were studied by SEM and MTT assay, respectively. Our results showed a good and remarkable mechanical strength, with Young's modulus values of 80±20 MPa and an ultimate strength of 18±2 MPa. Moreover, cell adhesion and proliferation were excellent, the cells appeared well spread and attached to the silkworm gut fibers surface, connecting to neighbouring cells and organizing a monolayer over the braided material at day 21 post-seeding. We conclude that silkworm gut fibers combine good mechanical and biological characteristics to be considered a potential biomaterial in tissue engineering applications.

Biography

Ana Pagán obtained a degree in Biology from University of Murcia. She has completed her PhD from the same university with a research stay at the Division of Nutrition and Metabolic Diseases, LMU University, Munich, Germany. She works as a Postdoctoral Researcher in the Imida Murciano Institute for Agricultural and Food Research and Development (IMIDA, Murcia, Spain), in the Department of Biotechnology, working on premier biomaterials in tissue engineering.

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Influence of selective laser melting mode on the structure and phase composition of Ti-Nb alloy

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Ti-Nb alloys are perspective for implants production. Titanium and its alloys have high elastic modulus (100-120 GPa). Due to their features alloys of Ti with (40-45) wt. % Nb have modulus close to that of bone. Selective laser melting (SLM) allows obtaining of low-modulus Ti-Nb alloys and items of complex shape. Change of SLM parameters affects the size of structural elements and phase composition of resulting product. The purpose of this study was to investigate influence of SLM parameter change on the structure and phase composition of Ti-(40-45) wt. % Nb alloy. 3-D specimens obtained in Yurga Institute of Technology (Russia) on "VARISKAF-100MVS" installation were investigated. To obtain the alloy the composite powder of titanium and niobium was obtained by mechanical activation of titanium and niobium powders mixture in AGO-2C ball mill (AltSTU, Barnaul, Russia) and was layered on titanium substrate. After activation composite powder was annealed in vacuum at 500°C during one hour. The thickness of each layer was 0.05 mm. Melting process was carried out in Ar atmosphere. Specimens were formed with the laser beam of 80 W-power. The spot diameter was 150 μm, scanning step was 0.4 mm. As a changed parameter laser beam scanning velocity was selected. It was changed in the range 40-70 mm/sec with the step of 10 mm/sec. The results of investigation have shown that the alloy obtained by SLM has an elemental composition of Ti-45 wt. % Nb. Powder is completely melted and crystallized during SLM. The structure is represented by two phases. They are the main β-solid solution of titanium and niobium and α"-Ti containing Nb. The microstructure contains zones with fine and medium grains. Shrinkage and gas pores are observed in specimens.

Biography

Margarita A Khimich graduated in Physics, and is a Technical Faculty of National Research Tomsk State University. She earned a Bachelor of Technical Physics in 2013. She presented her Master's thesis devoted to alloys of Ti-Nb system and severe plastic deformation of Ti-Nb alloy in 2015. Currently, she is a postgraduate student at National Research Tomsk State University and also a Researcher of the Laboratory of Physics of Nanostructured Biocomposites, Institute of Strength Physics and Materials Science. She takes part in the project of Russian Science Foundation devoted to selective laser melting of biocompatible Ti-Nb alloys.

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Silk fibroin nanoparticles as an efficient carrier for quercetin

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In the last decades, several researchers have associated a flavonoid-rich diet with an increase in average life in Mediterranean area and a related reduction in the frequency of cardiovascular diseases. Up to date, multiple formulations with different encapsulation methods and carriers for Q have been described in order to improve the stability and bioavailability of flavonoids. This work describes how silk fibroin nanoparticles (SFNs) are capable of adsorbing and releasing quercetin and how their integrity is highly preserved when is adsorbed onto the nanoparticles, as confirmed by antioxidant activity assays. Quercetin loading onto SFNs was optimized in terms of quercetin/SFNs ratio (w/w), time of adsorption and solvent mixture. Quercetin-loaded silk fibroin nanoparticles (QSFNs) were characterized using the dynamic light scattering technique to measure the diameter (Z-Average) and Z-potential (ζ). The size of loaded particles reached 171±1 nm (PdI=0.190) and were slightly bigger than the empty SFNs 139±1 nm (PdI=0.158), while the ζ potential of QSFNs in water shifted toward positive values, from –27.3±0.4 mV in empty SFNs to –17.1±2.4 mV in QSFNs. Protein corona formation onto SFNQs was lower when the loaded quercetin increased due to the shielding effect of the flavonoid around the nanoparticles. The antioxidant activity against DPPH• showed that the Q loaded in QSFNs not only retains the antioxidant activity but also has a synergistic scavenging activity due the intrinsic antioxidant activity of the silk fibroin. Drug loading content (DLC) and Encapsulation Efficiency (EE) varied with the relation between Q and SFN in the loading solution reaching a maximum values of EE=70% and DLC of 0.7%. The sustained release of Q was observed during the experiment both in phosphate buffer saline pH 7.4 and simulated intestinal fluid pH 6.8 with an overall cumulative release of 40% after 24h. SFNQs fluorescence can be detected in a L929 cell. The results point to SFNs as promising candidate for Q loading, transport and delivery with potential applications in nanomedicine, while retaining their nano-size and their antioxidant properties.

Biography

Antonio Abel Lozano-Pérez completed BSc degree in Biochemistry and Chemistry from University of Murcia, Spain and gained a PhD in Chemistry from University of Murcia, Spain. In 2010, he gained a position as PhD researcher in the Biotechnology Department of the IMIDA (Murcia, Spain) to develop new applications of the silk fibroin nanoparticles. He has his expertise in chemistry of the silk fibroin and in processing the silk to obtain nanoparticles for drug loading and delivery useful for nanomedicine. He has developed these nanoparticles after years of experience in research and development, both in the University of Murcia and IMIDA Institutions.

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Electrical stimulation of PC-12 cells cultured on silk fibroin scaffolds coated with reduced graphene

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New approaches to neural research require biocompatible materials capable to act as electrode structures or scaffolds in order to stimulate or restore the functionality of damaged tissues. Graphene is a conducting material introduced in the field of tissue engineering due to its good biocompatibility and potential applications in biomedicine. Silk fibroin (SF) is also a well-known biocompatible material in itself that combines with graphene producing hybrid films formats, providing an excellent support for cell proliferation. However, the use of electrospun mats seems to be a better choice due to the biomimetic configuration with an extracellular matrix. Therefore, the approach proposed in the present work explores the combination of reduced graphene oxide (rGO) adsorbed onSF mats in order to confer them electroconductive properties. PC-12 cell line was chosen for the study since these cells can be differentiated into a neuronal-like phenotype by exposing to NGF. The differentiation levels achieved with this treatment (SF/rGO/NGF) were compared to the ones obtained in cells growing on: Pure SF mats (SF), mats coated with rGO submitted to Electrical Stimulation (SF/rGO/ES) and mats coated with rGO without any other stimulus (SF/rGO). The method of production of these scaffolds barely alters the mechanical properties of pure SF mats. However, multiple benefits are obtained by means of the coating with rGO. In addition to the optimal viability detected in cells growing on all the produced materials, a clear improvement of adhesion and proliferation is exhibited in mats containing rGO. The stimulus provided by the rGO itself induces a significant differentiation level to neuronal-like phenotypes. However, the percentage of differentiation can be increased by means of the application of ES (100 mV during 2h) or the treatment with NGF, being the neurite outgrowth more pronounced when electric currents are applied to the cell cultures.

Biography

Salvador Aznar-Cervantes works as a Researcher in the Department of Biotechnology in the R&D Center in Biotechnology and Biomedicine, IMIDA (Murcia). He obtained his Degree in Biology from the University of Murcia (2006), then he completed his Doctoral thesis, working as a Grant Holder (FPI-INIA), under the guidance of Dr. José Luis Cenis Anadón, in January 2013. While he is pursuing his PhD, he researched on biotechnological and biomedical applications of the silk worm (Bombyxmori). This period was complemented with 3 successive visits (2010, 2011, and 2012) to the Department of Chemical Engineering of Massachusetts Institute of Technology (MIT), where he also collaborated with Tufts University (Professor David L Kaplan) and the Massachusetts General Hospital (Professor Robert Redmond).

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Production of bone tissue support materials based on bioactive glass-polymer composites

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Bone tissue support materials have biocompatibility, biodegradability and bioactivity that are made of various ceramics, polymers or both of ceramics and polymers which are called composites. The most interesting of them are bioactive glasses due to their excellent features. Bioactive glasses are osteoconductive and osteoinductive materials and when they are implanted on bone, they connect to the bone tissue. They are generally used in order to fill bone defect and promote new bone formation because of their osteogenic cell stimulator and bioactive properties. In recent years, bioactive glass materials which are used as bone in the form of block, granules, injectable or paste has increased significantly. These forms which are called support materials make patient healing and surgical operation easier. In this study, injectable bone tissue support materials based on bioactive glass-polymer composites were produced for bone tissue engineering applications. At different ratios of bioactive glass and alginate composites were prepared such as 1:1, 1:2 g/ml, respectively. All samples were characterized by Fourier Transform Infrared Spectroscopy (FT-IR) and X-Ray Diffraction (XRD) analysis before simulated body fluid (SBF) to understand structure of composites and after SBF to understand bioactivity properties of composites.

Biography

Ali Can Özarslan completed Bachelor's degree at Yildiz Technical University, Department of Bioengineering in 2015. He continues his education as a Graduate Student at Yildiz Technical University, Department of Bioengineering. He has 2 research papers published by the international refereed journals and 5 papers published by the international scientific meetings. Topics of his interest are Bone Tissue Engineering, Biomaterials, and Bone Tissue Support Materials.

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Biological properties of a new Si-Ca-P porous scaffold for tissue engineering

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In the last few decades, life expectancy of the population has increased as a consequence of health improvements, increasing the incidence of bone problems, like fractures, osteoporosis and bone metastasis. Traditionally, these bone lesions are treated by reconstructive surgery, using autologous, allogeneic or xenogeneic implants, having the problems of lack of donated organs and tissues as well as the immune rejection. For this reason, the emergence of tissue engineering was necessary. This science studies how to achieve the regeneration of diseased tissues using scaffolds with appropriate physical and biological properties. Silicon (Si) is a trace element that enhances bone formation and maturation in the body. Therefore, in this work, an 85 wt% C2S-15 wt% TCP porous scaffold has been studied for future medical uses. The porous scaffolds were produced by the polymer replication method using polyurethane sponges with open cells as a template. They were impregnated with appropriate ceramic slurry and sintered. After obtaining the porous scaffold, ions release was performed to know their behavior in DMEM, cytotoxicity and metabolic activity assays were carried out to know their biocompatibility with adult human Mesenchymal Stem Cells (ahMSC) and, finally, FESEM images were obtained to observe the morphology of the ahMSC over the surface of the material. The exchange of ions between the media and the material was good and the rest of experiments showed a low cytotoxicity and a good metabolic activity of the ahMSC, as well as a good morphology of the cells over the surface of the material at different times. We can conclude that these scaffolds could be a good option for future uses in regenerative medicine, although more *in vitro* and *in vivo* experiments will be necessary to complete this study.

Biography

Patricia Ros-Tárraga completed her Graduation at Universidad Miguel Hernández of Elche (UMH). Currently, she is pursuing her Pre-doctoral studies at Universidad Católica San Antonio de Murcia (UCAM), and working in the design and development of new bioactive materials and their use in the field of Bone Tissue Regeneration. She studies the physical properties of Si-Ca-P-based scaffolds and their effect on the adult human Mesenchymal Stem Cells (ahMSC) behavior.

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Nurse's A-phase material enhance adhesion, growth and differentiation of human bone marrow-derived stromal mesenchymal stem cells

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Silicon (Si) is a trace element that enhances bone formation and maturation in the body; thus apatite ceramics containing Si are expected to increase the speed of bony regeneration. The mesenchymal stem cells from human bone marrow (*ah*MSCs) are a great promise for cell-based therapies by their ability to differentiate into osteoblast in certain microenvironments. The purpose of this study was to evaluate the effect of a well-characterized Nurse's A-phase (7CaO·P2O5·2SiO2) ceramic compared to a control (tissue culture polystyrene-TCPS) on osteogenic differentiation of *ah*MSCs *in vitro*. Alizarin Red-S (AR-s) staining, alkaline phosphatase (ALP) activity, and collagen I (COLI) were evaluated. Also, field emission scanning electron microscopy (FESEM) images were acquired in order to visualize the morphology of the cells. The entire surface was colonized after 28 days of culture in growth medium (GM). Osteoblastic differentiation markers were significantly enhanced in cells growing on Nurse's A phase ceramic and cultured with osteogenic medium (OM), and cells acquired polygonal shape typical from osteoblasts, probably due to the role of silica to stimulate the differentiation of *ah*MSCs. Moreover, calcium nodules were formed under the influence of ceramic material. Therefore, it is predicted that Nurse's A-phase ceramic would present high biocompatibility and good osteoconductivity, being a good candidate to be used as a biomaterial for bone tissue engineering.

Biography

Rubén Rabadán Ros is a Biologist at the University of Murcia (UMU). He completed his MSc degree in Molecular Biology and Biotechnology from the same University. Currently, he is a PhD student in Biomedical Sciences at Universidad Católica San Antonio, Murcia (UCAM), developing scaffolds based on the C2S-TCP phase diagram and their *in vitro* and *in vivo* study.

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Sun light exfoliated reduced graphene oxide loaded isabgol scaffolds accelerates collagen synthesis, vascularization and wound healing in diabetic rats

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Statement of the Problem: Diabetes mellitus (DM) is one of the major health concerns with increasing prevalence. Wounds in diabetic patients are slow to heal and persist for few months under proper wound care and management. Pathophysiology of impaired diabetic wound healing is still unclear and it is presumed that delayed healing is due to the persistence of prolonged inflammation and an inadequate angiogenic response. However, an ideal wound dressing material can act as a protective barrier against pathogens, help in cell attachment, proliferation, migration and differentiation during wound healing process.

Methodology: Fabrication of the reduced graphene oxide loaded isabgol (Isab) scaffolds (Isab/rGO) was prepared by freeze drying method using STMP crosslinking. Biocompatibility of the Isab/rGO scaffolds was carried out in NIH 3T3 fibroblast cells. Then, these scaffolds were used as a topical wound dressing material to assess the normal and diabetic wound healing efficacy using 2×2 cm^2 full thickness open excision wounds in Wistar rats. Granulation tissue collected from wounds was used to evaluate the biochemical, biophysical, histopathology and immunohistochemistry analyses.

Results: Isab/rGO scaffolds are biocompatible in NIH 3T3 L1 cells and it also showed significant antibacterial activity. Isab/rGO scaffolds treatment showed increased wound contraction ($p<0.05$) compared to control and isab scaffold both in normal and diabetic wound healing. Period of epithelialization is also significantly reduced in isab/rGO scaffolds treated normal and diabetic wounds compared to isab and control. Histopathology and immunohistochemistry results also revealed that the isab/rGO scaffold dressing accelerated macrophage recruitment and neovascularization to heal the wounds faster.

Conclusion & Significance: These results demonstrated that incorporation of rGO in isabgol can reduce the prolonged inflammation and enhance the wound healing by accelerating the neovascularization and collagen synthesis. Hence, isab/rGO scaffold could be an inexpensive wound dressing material for diabetic wound healing application.

Biography

Thangavel Ponrasu has completed his MSc, MPhil and PhD in Biochemistry. He has expertise in diabetic wound healing. During his PhD, he has gained hands on experience in toxicity evaluation in zebra fish embryos and screening medicinal plants for diabetic wound healing. Currently, he is pursuing his Post-doctoral research in the Department of Biotechnology, IIT Madras, India from July 2014. During his Post-doc, he is developing novel, inexpensive wound dressing materials to enhance diabetic wound healing. He has published 22 papers in peer reviewed journals so far. He has attended many national and international conferences to present his research findings. He is focusing on the development of inexpensive wound dressing materials to heal the diabetic wounds much faster.

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Quantitative accurate mechanical measurements with atomic force microscopy new techniques for studying biomaterials

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Atomic Force Microscopy (AFM) is a powerful imaging technique that has also emerged as an indispensible technique for measuring mechanical properties of biomaterials and biological samples. It provides high spatial resolution and force sensitivity within physiologically relevant environments in the kPa to GPa elastic modulus range. To respond to the large diversity of material properties a variety of AFM techniques can provide the most relevant or accurate data for every application. Here we are reviewing a large number of available techniques and how they apply to different types of biomaterials, as well as different stages of fabrication, quality control and testing. In particular we will review and compare the following techniques: Force Curve Measurements, Fast Force Mapping, Phase Imaging, Loss Tangent Imaging and AM-FM (Amplitude Modulation-Frequency Modulation). AM-FM mode, for example, delivers high-resolution topographical images and simultaneously measures quantitative contact stiffness data, from which elastic modulus can be calculated with appropriate models for the tip-sample contact mechanics. With the growing demand for mechanical characterization of materials at the nanoscale, the AM-FM technique provides quantitative nanomechanical information, while simultaneously offering all the familiar advantages of tapping mode. Together all these AFM different techniques can be used on any biomaterial and measure a wide range of properties including elastic stiffness, loss and storage modulus, viscous damping, adhesion, and hardness. This short review should help determining which technique to choose based on the research goals and the samples.

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Structure and properties of nanocrystalline chitosan

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Chitosan and its derivatives are polymers with excellent properties to be used in regenerative medicine because they guarantee efficiency in the healing process. This polymer has a great potential for the development of a new generation of biomaterials that can be used in regenerative medicine and tissue engineering. The nanocrystalline chitosan (nCh) is a modified form of chitosan prepared by the method of obtaining chitosan salts. It is characterized by having the same special properties of the precursor chitosan as biocompatibility, bioactivity, be non-toxic and biodegradable. The aim of this study was to develop a new method of obtaining nanocrystalline chitosan according to their chemical and physical characterization. The material was characterized by Absorption Spectroscopy in the Infrared Region - with the Fourier transform (FTIR - ATR), scanning electron microscopy, SEM, Nuclear Magnetic Resonance, NMR, Diffraction of X-rays, particle size analysis and the potential Zeta. The results indicated that the process of obtaining nanocrystalline chitosan, did not change the structure of the precursor chitosan. The analysis in the FTIR showed the same functional groups of the precursor chitosan. The 1H-NMR spectroscopy was helpful in the analysis of the chitosan samples in a wide range of values to determine the degree of deacetylation (GD). The morphology indicates the homogeneity of the structure and the surface. The X-ray diffraction shows the reduction of crystallinity of QNC, which corresponds to the amorphous structure thereof. The value of the zeta potential of the chitosan acetate (AQ) in acid media (pH 4.43) was 43.6 mV, while the value of QNC (pH 7.3) was 15.4 mV due to its high polydispersity. The variation in particle size of samples, and AQ using QNC 0.450 uM mesh filter, indicated the average particle size of 55.52 and 266.0 nm, respectively.

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Living implant fortified with active therapeutics and well organized stem cells for regenerative nanomedicine

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Recently, we have reported an active nanostructured collagen implant reinforced with human stem cells for bone regeneration. In our group, we have reported smart hybrid materials equipped with nanoreservoirs of therapeutics and stem cells spheroids. This unique nanotechnology strategy is used to entrap, protect, and stabilize therapeutic agents into polymer coatings acting as nanoreservoirs enrobing nanofibers of implantable membranes. Upon contact with cells, therapeutic agents become available through enzymatic degradation of the nanoreservoirs. As cells grow, divide, and infiltrate deeper into the porous membrane, they trigger slow and progressive release of therapeutic agents that in turn stimulate further cell proliferation. This constitutes the first instance of a smart living nanostructured hybrid membrane for regenerative medicine. The cell contact-dependent bioerodable nanoreservoirs described here will permit sustained release of drugs, genes, growth factors, etc., opening a general route to the design of sophisticated cell-therapy implants capable of robust and durable regeneration of a broad variety of tissues.

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Challenges to nanoscience and nanotechnology: Intriguing nanosize effect and nanotime effect

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We first introduce a novel nanosize concept and a novel "nanotime" concept along with reviewing a series of novel phenomena and novel techniques related to nanosize effect and ultrafast process, which were recently discovered in our lab or were reported in literature. In these concepts, for the first time we are able to account for the non equilibrium, amorphous-like, and nonlinear nature of the current nanoscience and nanotechnology. In particular, we demonstrate that the structure instabilities of materials occur when a material system is limited to a space within a scale that is comparable to atomic distance. Such a nanosize effect is crucially dependent only on the nanosize, but also on nanoshape or nanocurvature (including positive nanocurvature and negative nanocurvature). We also demonstrate that the structure instabilities of materials occur as well when the exchange of external energy with materials is limited to a time within a scale that is comparable to atomic vibration period. Such a "nanotime" effect can give rise to either soft mode or instability of atomic vibration in a condensed matter. The new concepts are very meaningful for control over fabrication and energetic beam processing of low dimensional nanostructures and nanodevices, especially for several potential applications related to nanoparticles, nanocavities, carbon nanotubes and nanowires. The new concepts have similarly important implications for chemistry, biology, and medicine as demonstrated by immerging new findings about nanocavities and nanolaser irradiation. In particular, in biology and medicine, there are widespread research interests either in using nanocavity (shell-core) structure to design and build biology composites, biosensors, drug deliverer, and protein structures or in nano surgery via ultrafast nanolaser processing, both being operative at the molecular level dealing with the concepts put forward herein.

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Bioceramics from calcium orthophosphates

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Various types of grafts have been traditionally used to restore damaged bones. In the late 1960's, a strong interest was raised in studying ceramics as potential bone grafts due to their biomechanical properties. A bit later, such synthetic biomaterials were called bioceramics. In principle, bioceramics can be prepared from diverse materials, but this review is limited to calcium orthophosphate-based formulations only, which possess the specific advantages due to the chemical similarity to mammalian bones and teeth. During the past 40 years, there have been a number of important achievements in this field. Namely, after the initial development of bioceramics that was just tolerated in the physiological environment, an emphasis was shifted towards the formulations able to form direct chemical bonds with the adjacent bones. Afterwards, by the structural and compositional controls, it became possible to choose whether the calcium orthophosphate-based implants remain biologically stable once incorporated into the skeletal structure or whether they were resorbed over time. At the turn of the millennium, a new concept of regenerative bioceramics was developed and such formulations became an integrated part of the tissue engineering approach. Now calcium orthophosphate scaffolds are designed to induce bone formation and vascularization. These scaffolds are often porous and harbor different biomolecules and/or cells. Therefore, current biomedical applications of calcium orthophosphate bioceramics include bone augmentations, artificial bone grafts, maxillofacial reconstruction, spinal fusion, periodontal disease repairs and bone fillers after tumor surgery. Perspective future applications comprise drug delivery and tissue engineering purposes, because calcium orthophosphates appear to be promising carriers of growth factors, bioactive peptides and various types of cells.

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Nanolipoblockers: Biomaterial therapeutics aimed at the ground zero of atherosclerosis and heart disease

Prabhas V Moghe
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Statement of the Problem: The uncontrolled accumulation of oxidized low-density lipoproteins (LDL) within the walls of blood vessels, called atherosclerosis, lies at the core of cardiovascular diseases and causes a staggering toll on adult mortality and rising health care costs.

Methodology & Innovation: Biomaterials as anti-atherosclerotic therapeutics for inhibiting cholesterol accumulation and the related inflammation. A generation of unimers whose surface features such as surface anionic density; amphiphilicity; and nanoscale architecture can be systematically varied was designed. Competitive binding to scavenger receptors was used as a key mechanism of action. Serum-stable nanoparticles were fabricated from the unimers using flash nanoprecipitation and the NLB nanoparticles were administered *in vivo* to treat the progression of atherosclerosis.

Findings & Conclusions: We report that assemblies of such nanolipoblockers (NLBs) can systematically block the scavenger receptor molecules that traffic highly oxidized LDL into macrophages and inhibit the resulting atherogenic phenotype. In parallel, a multimodal strategy of depleting cellular cholesterol was examined by using the NLBs as drug delivery carriers *in vivo*. The NLBs lowered intimal levels of accumulated cholesterol and inhibited macrophage retention relative to non-treated controls. A number of more recent project directions, including studies of molecular mechanisms of action, design of more stable nanoparticle formulations of the NLBs, and emergent pathways for translational medicine will also be highlighted in this talk.

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Materials based on thermoplastic starch as polymeric matrix

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Starch has been considered as one of the most promising bioplastics primarily because of its attractive combination of availability and price. Thermoplastic starch (TPS) can be obtained by destruction of starch granules in the presence of plasticizers under specific conditions. Polyols such as glycerol, glycol, sorbitol, and sugars are the most widely used plasticizers. The main disadvantages of TPS consist in pronounced hydrophilic nature, the fast degradation rate and, in some cases, unsatisfactory mechanical properties. In spite of some industrial applications of TPS exist, high volume production of TPS-based materials is rare at present and occurs only in exceptional cases for non-demanding products. In this lecture the principles for substantial improvement of ultimate propereties of TPS are discussed. A number of possible modifications have been investigated to affect the mechanical properties, water uptake, and the structure of the materials. The experiments were aimed to the optimization of the ratio of amylose and amylopectin, selection of appropriate plasticizers including their mixtures, modification of hydrophilicity by chemical modification of hydrophobic functional groups or via crosslinking of TPS, and mixing the TPS with hydrophobic biodegradable polymers added as the minor component. In most cases the optimization resulted in a substantial changes of properties of TPS-based materials. The possible routes are discussed resulting in modified starch- based materials being able to compete with standard plastics in more demanding applications.

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Conducting biomaterials for regenerative medicine

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Electrical fields play important roles in a multitude of biological processes, which has inspired the development of electroactive biomaterials (e.g. bionic ears/eyes, cardiac pacemakers, neural electrodes), some of which have been clinically translated. The tuneable properties of conducting electroactive polymers (CPs or EAPs, respectively) such as derivatives of polyaniline, polypyrrole or polythiophene make them attractive components of biomaterials for drug delivery devices, electrodes or tissue scaffolds. With a view to develop conducting polymers for drug delivery, we have developed solution processable polymers (e.g. block copolymers, supramolecular polymers) on a multigram scale, loaded them with a clinically relevant drug and studied its delivery in the absence/presence of electrical stimulation, and such systems offer a route to triggering the delivery in response to electricity. Likewise, with a view to develop tissue scaffolds, we have developed polymer-based materials with various morphologies (e.g. films, fibers, foams) that were electrically conductive with derivatives of polypyrrole or polythiophene. The cells were cultured (human stem cells, human fibroblasts, or rat Schwann cells) thereon and their behaviour was studied in the absence/presence of electrical stimulation, observing enhancement of stem cell differentiation towards osteogenic outcomes, or increased nerve growth factor production from Schwann cells, when exposed to electrical stimuli. I will present the most recent developments from my group.

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Elastin-like recombinamers as advanced biomaterials for biomedical applications

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Elastin-like recombinamers, ELRs, are a class of polymeric material whose composition is bioinspired in natural elastin and obtained by recombinant DNA technologies. Their tailor made design allows to include, with a complete sequence control, both functional groups and bioactive domains specifically for each application. These biomaterials are characterized by their biocompatibility, biodegradability, stimuli responsiveness, self-assembly and excellent mechanical properties. Their thermoresponsiveness has allowed us to obtain nanoparticles like nanovesicles for tuberculosis vaccine from elastin-like block core combinamers. Other nanostructures for intracellular gene delivery applications, design from ELRs and aptamers, are polyplexes that protect therapeutic DNA and act as non-viral cell type specific vectors in breast cancer therapy. Drug controlled release has been also tackled by elastin-based hydrogels formed from thermogelificable ELRs for glaucoma treatment. Their adequate mechanical properties have allowed them to have been electrospun to form fibers and micropatterned to give hydrogels with different and reliable topographies, necessary for the study of cell behavior, with proved moldability. Moreover, ELRs biofunctionalized surfaces are especially useful for implant biocompatibility and, as smart surfaces, for cell and cell-sheet harvesting once exploiting their self organized nanostructure with temperature that makes these thermoresponsive surfaces to switch between cell adherent and non adherent states to be applied as a reliable way to harvest different cell lines. Chemically crosslinked ELRs hydrogels have been obtained by clean, fast and atom economy click methodology, and *in vitro* assays for cellular adhesion and proliferation with different cell lines confirm their viability and bioactivity. ELRs hydrogels have been used for different biomedical applications as implant recoveries or as injectable hydrogels at physiological conditions. Within the field of tissue engineering, they have been applied for cartilage regeneration or for osteochondral bone tissue defects repairing.

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Self-assembling bioactive peptide-ELP fusion protein nanoparticles for wound healing and regenerative medicine

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A number of skin substitutes have been developed over the years to promote wound healing in acute and chronic wounds. While it has been proposed that the addition of growth factors and other agents could improve the efficacy of healing and regeneration, this strategy does not work because purified peptide growth factors are short-lived in the highly proteolytic wound environment. To address this limitation, we have developed long-lived nanoparticle technologies that can release bioactive peptides to help improve wound healing. These nanoparticles consist of fusion proteins of elastin-like peptides (ELPs) fused with relevant bioactive peptides that spontaneously self-assemble at physiological temperatures. The technique used enables rapid and inexpensive purification of the fusion proteins through inverse transition cycling, and the nanoparticles thus formed are small enough to be easily incorporated into existing skin substitutes. Results will be shown using three different bioactive peptides: ARA290, SDF-1 and KGF. ARA290 is a peptide from erythropoietin that increases the tolerance of cells to stress, and helps preserve functionality of the microvascular network around the primary injury. SDF-1 is a growth factor that has been shown to inhibit wound contraction and promote dermal regeneration *in vivo*. KGF is known to stimulate epidermal cell proliferation and migration; Due to the versatility of the ELP-based technology, one can develop ELP fusion proteins that target many different aspects of the healing process. Although here we chose to target cell viability (ARA290), the dermis (SDF-1), and the epidermis (KGF), once could consider ELP-based nanoparticles that incorporate other peptides secreted by M2 macrophages, such as TGF-beta and IL-10, as well as cationic bactericidal peptides. The nanoparticles may also be useful in a variety of applications to treat injuries to tissues other than skin, where in many instances pre-formed or injectable matrices are used to promote tissue repair and regeneration.

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Parametric designs based on CFD for a new generation of ventricular catheters for hydrocephalus

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Background: To drain the excess of cerebrospinal fluid in a hydrocephalus patient, a catheter is inserted in one of the brain ventricles, and then connected to a valve. This so-called ventricular catheter is a standard-size, flexible tubing with a number of holes placed symmetrically around several transversal sections or "drainage segments". Three-dimensional computational dynamics shows that most of the fluid volume flows through the drainage segment closest to the valve. This fact raises the likelihood that those holes and then the lumen get clogged by the cells and macromolecules present in the cerebrospinal fluid, provoking malfunction of the whole system.

Objective: To better understand the flow pattern, we have carried out a parametric study via numerical models of ventricular catheters.

Methods: The parameters chosen are the number of drainage segments, the distances between them, the number and diameter of the holes on each segment, as well as their relative angular position.

Results: These parameters were found to have a direct consequence on the flow distribution and shear stress of the catheter. As a consequence, we formulate general principles for ventricular catheter design. To exclude the drainage area of the segments from the set of parameters, the drainage areas of the distal segment, and the proximal segment, were conveniently chosen in each group, while the drainage areas of the remaining segments.

Conclusions: These principles can help develop new catheters with homogeneous flow patterns thus possibly extending their lifetime.

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Characterization of biomaterials using AFM based fast nanoscale imaging and quantitative nanomechanical techniques

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Besides structural and physico-chemical composition, topography, roughness, adhesiveness as well as mechanical properties of biomaterials are the relevant factors making them suitable for biomedical applications. All these factors affect cell differentiation and tissue formation, and are crucial for their integration as well as healing capacity in the human body. Atomic Force Microscopy is suitable for measuring all of these characteristics with nanometer scale resolution under physiological conditions. We have developed a multipurpose AFM device allowing comprehensive characterization of biological samples such as live cells, tissues and biomaterials in the nanoscale. True optical integration allows the simultaneous use of advanced inverted optical microscope techniques such as DIC or confocal laser scanning microscopy, but also upright optics, such as macroscopes for the investigation of opaque samples. With our "Quantitative Imaging" (QI™) mode several sample properties, such as the topography, stiffness and adhesiveness, can be obtained with one measurement in high resolution. Even more complex data like Young´s modulus images, topography at different indentation forces in terms of tomography, or recognition events can be obtained. A variety of biological samples have been investigated to demonstrate the capability and flexibility of QI™. The NanoWizard® ULTRA Speed technique allows fast AFM imaging of dynamic processes with approximately 1 frame per second. The kinetics of collagen type I fibrillogenesis was imaged *in situ* with high spatiotemporal resolution, revealing the formation of the 67 nm D-banding hallmark. With the CellHesion® technique, the adhesion of a single living cell to any substrate can be measured and validated using comprehensive analysis tools. The side-view cantilever holder enables a side view of the cell-sample interface while performing adhesion experiments, providing complementary information without expensive z-stacking. The inherent drawbacks of traditional AFM imaging modes for fast imaging or for challenging samples like living cells can be overcome by the NanoWizard® ULTRA Speed and QI™ mode. We present an enhancement of the AFM technique providing a versatile tool for an extensive characterization of biomaterials.

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Design and fabrication of a novel meniscal prosthesis

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Statement of the Problem: The motivation for the design of the novel meniscal implant was based on the collagen fibre orientation in the native meniscus, which is the dominant component of the native meniscus. The architecture of the meniscus is such that the collagen fibre bundles wound circumferentially, and are responsible for the complex multifaceted load bearing nature; while a small number of radially orientated collagen fibres function like a fastener for the circumferential fibres, providing support and preventing them from splitting under loading conditions. Polymeric composite biomaterials are both anisotropic and heterogeneous which are the properties of the natural meniscus. A combination of the circumferential and radial reinforced fibres in a matrix is therefore anticipated to produce an enhanced final outcome. The development and fabrication of such an artificial composite structure with both circumferential and radial oriented fibres is complicated and is therefore a challenge.

Materials & Methods: Bionate PCU 80A and 90A pellets, and Dyneema Purity® UG fibres. The prostheses were fabricated in a two-stage injection moulding process. A mini bench-top injection moulding machine was designed and fabricated for this purpose.

Findings: With some moulding challenges overcome, the process proved to be a successful means of producing the meniscal composite prostheses with reinforcement fibres orientated both circumferentially and radially in the PCU matrix.

Conclusion: A manually operated injection moulding machine has been designed and fabricated for manufacturing the prostheses. Having overcome the limitations of the manual equipment, it could be said that the method if revised and automated could be a feasible means by which the prostheses can be produced for clinical applications.

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Conducting polymer based composites as scaffold for tissue engineering application

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Stimuli-responsive polymers are special class of polymeric materials which can respond to even very slight changes in temperature, pH, light, and ionic strength, have been widely utilized in tissue engineering, drug delivery systems and sensors. Temperature change is a widely observed phenomenon in the physiological systems. Temperature-sensitive materials have attracted significantly owing their ability of intelligent response to temperature changes. The most challenging aspect in the temperature controlled cell adhesion is the development and design of 3D scaffolds which should provide a suitable and proper environment for easy attachment, proliferation, differentiation and detachment of cells. Poly (N-isopropylacrylamide) (PNIPAM) is a well-known and studied thermo responsive polymer. It exhibits a reversible phase transition between hydrophilicity and hydrophobicity because of intermolecular and intramolecular hydrogen bonding. Based on this mechanism, the poly (N-isopropylacylamide) based matrices could act as the controllable temperature-responsive bio-switches for biomedical and biotechnology applications. On the other hand, conducting polymers especially polyaniline has received much attention in recent past because of good processability, fast charge-discharge and biocompatibility. When fibroblast cells were seeded on the nanofibers surface, the PANI-PNIPAm composite nanofibers exhibited highest cell growth and %live of around 98% indicating very good biocompatibility and possible use of these nanofibers as scaffold for the tissue engineering application recognition.

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Polymer electrode material for microbial bioelectrochemical systems

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Bioelectrochemical systems based on polymer-bacteria thin film modified electrode were explored. The prepared polymer-bacteria modified copper electrode was characterized with voltametric methods, as cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS). The proposed electrode indicated a definite redox response, high conductivity and electrochemical stability. The experimental results revealed that the prepared electrode could be a feasible for degradation of hazardous phenol pollutants. Oxidation of phenol was invested by cyclic voltammetry and EIS. EIS diagrams resulted in separate time constants; the oxidation of phenol is mostly represented by half a circle, whose diameter corresponds to the electron transfer resistance. Electron transfer resistance produced by polymer-bacteria modified copper electrode is less than that obtained by polymer modified copper electrode.

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Synthesis and solubilization of flurbiprofen derivatives and investigation of their biological activities

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Flurbiprofen is one of the most potent non-steroidal anti-inflammatory drugs. It is widely used for relief of pain in patients suffering from rheumatic diseases, migraine, sore throat and primary dysmenorrhea. However, its aqueous solubility is very low and hinders the skin permeation. Thus, it is imperative to develop such a drug delivery systems which can improve its aqueous solubility and hence improve the skin permeation and therapeutic compliance. Micro-emulsions have been also proven to increase the cutaneous absorption of lipophilic drugs as compared to conventional vehicles. Micro-emulsion is thermodynamically stable emulsion that has the capacity to 'hide/solubilize' water-insoluble molecules within a continuous oil phase. Therefore, flurbiprofen was converted to esters through chemical reactions with alcohols such as methanol, ethanol, propanol and butanol. The product was further treated with hydrazine to get hydrazide. The solubility of the parent drug flurbiprofen and the products were solubilized in micro-emulsions formed using various surfactants like ionic, non-ionic and zwitterions. It has been concluded that the product was more soluble than the parent compound. The biological activities of these were also investigated. The outcome was very promising and the product was more active than the parent compound. It therefore concluded that in this way we can not only enhance the solubility of the drug, increase its bioactivity but it also reduces the risk of stomach cancer.

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Innovation & sustainability in the contemporary fashion

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On the dynamic business scenario, be functional, smart and interactive are the most valuable asset to become a reference in our markets. The global smart textile market promotes the implementation of nanotech and biocomposites projects in this field. Please note the market by moving beyond traditional path of what means value and fulfilling business future. We can identify the strategic alliance between textile industry and several markets such as polymer, cosmetic, health, architecture and fashion. For several years, while these "S-textile" program have been able to go beyond the original objectives and is seeking its way towards industrialization and mass production for enhancing the breakthrough of intelligence textile systems. Every innovative initiative are committed in improving the convergence between industries and the leading edge of the textile market; in this scenario, the priority is deep understanding of megatrends and new segments. We discuss about the most important trends that will define the architecture future of Smart Textile world.

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Metallic biomaterials and surface functionalization of Ti based alloys for medical applications

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Metallic biomaterials are widely used in the manufacturing of medical devices for hard tissue replacement such as pace maker cases and screws to assist patients when their body parts are damaged. The basic information of three main categories of metallic implant biomaterials, stainless steel, cobalt and titanium (Ti)-based alloys are introduced in this paper. In addition to mechanical performance, the other essential requirements that are needed to be posted by these metallic biomaterials are also explained. Various advantages of using these metallic biomaterials as an implant and their current applications also are reviewed. The main issue during implantation of a biomaterial (i.e., Ti implant) and its alloys is inflammatory of surrounding tissues and eventually it leads to implant failure even when the biomaterial has shown excellent properties. This review paper covered some of the recent notable surface functionalization techniques and the obtained results contributed to biomedical field to resolve the problems. It firstly explained that the biocompatible metal layer (tantalum) is deposited onto bare Ti and Ti substrate with the nanoporous Ta-incorporated surfaces using various methods of deposition to improve the performance in terms of corrosion resistance and biological performances. Attachment of hydroxyapatite (HA) onto Ti surface is one of the ways of getting rid of the negative effects of Ti. However, HA has poor mechanical properties and low bond strength with Ti. Thus, a composite coating that can improve the lack of HA properties was formed. Moreover, the last investigations related to incorporating antibacterial nanoparticles and drugs with Ti implants are presented, as well. The overall results indicated that the antibacterial performance of Ti implants improved with attachment of incorporating antibacterial agents onto it. Carbon nanotubes (CNTs) and biocompatible polymers are integrated onto Ti to improve the cells adhesion and growth as well as reducing the toxicity which will lead to the longevity of implants. The investigator studies are revealed that the different surface properties on Ti will affect the absorption of protein and increase of biocompatibility.

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Development of an *in vitro* testing battery to assess biocompatibility of medical devices

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In order to guarantee safety for the end-users of medical devices, they have to be tested for adverse reactions on the skin before market authorization. Animal testing is still state of the art, but ethically questionable and expensive. During the last years, socio-political pressure has led to the development of alternatives. One of the key aspects of our recent research is to establish an *in vitro* testing battery to examine the biocompatibility of medical devices in contact with the skin or mucosa. The first task was the development of an appropriate extraction method in order to cover a wide range of substances migrating from the device. As skin models and various assays have already been developed for testing pure chemicals, the focus was on the establishment of such methods to assess extracts for cytotoxicity, irritation and sensitization. To identify a possible sensitization potential, a screening method to cover different steps of the skin sensitization process was developed. The molecular initiation event, the binding of haptens to peptides can be assessed by chromatographic methods. The molecular and cellular responses include the activation of an antioxidant pathway in keratinocytes and hence, activating the phenotypical deformation of dendritic cells. So far, various samples have been examined in the different assays. Spiking of sample extracts was used to prevent false negative results. Additionally, samples were examined with animal testing in order to compare the results which showed more sensitive responses in the *in vitro* assays. Further, it could be shown that not only materials themselves but also the manufacturing process plays an important role for biocompatibility. In this context, production processes of medical devices were improved. Summarizing, these assays are developed not only with a sufficient sensitivity, but also to be robust, simple to use, ethically responsible and inexpensive in comparison to current animal testing.

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