BOOK of ABSTRACTS

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21-26. June. 2015

Milocer, Hotel Maestral, Montenegro

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International Journal of Nanomedicine

ISSN: 1178-2013

Editor-in-Chief: Dr Thomas J Webster

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I – PLENARY TALK

II – INVITED TALK

III – ORAL PRESENTATION

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ISBN 978-86-7236-089-9

15 YEARS OF CONDUCTING NANOMEDICINE RESEARCH: WHERE ARE WE HEADED?

Thomas J. Webster

Arthur W. Zafiropoulo Chair and Professor, Chemical Engineering, Northeastern University and Center of Excellence for Advanced Materials Research, King Abdulaziz University, Saudi Arabia

There is an acute shortage of organs due to disease, trauma, congenital defect, and most importantly, age related maladies. The synthetic materials used in tissue engineering applications today are typically composed of millimeter or micron sized particles and/or fiber dimensions. Although human cells are on the micron scale, their individual components, e.g. proteins, are composed of nanometer features. By modifying only the nanofeatures on material surfaces without changing the surface chemistry, it is possible to increase tissue growth of any human tissue by increasing the endogenous adsorption of adhesive proteins onto the material surface. In addition, our group has shown that these same nanofeatures and nano-modifications can reduce bacterial growth without using antibiotics, which may further accelerate the growth of antibiotic resistant microbes. Finally, nanomedicine has been shown to stimulate the growth and differentiation of stem cells, which may someday be used to treat incurable disorders, such as neural damage. This invited talk will highlight some of the advancements and emphasize current nanomaterials currently approved by the US FDA for human implantation.

 ISBN 978-86-7236-089-9

WATER BASED NANOMEDICINE: DIAMAGNETIC/PARAMAGNETIC PROPERTIES OF WATER, HEALTHY AND UNHEALTHY BIOLOGICAL TISSUES

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In comparison with other natural molecules and substances, water possess about forty physicochemical anomalies. Regardless that water is major component of living systems. For many years there is a controversy about biological water properties in comparison to bulk water. Key point for understanding these differences is collective phenomena of water covalent and non-covalent hydrogen bonds and its interactions with DNA, proteins and ions.

It is well known that single water molecule is diamagnetic having magnetic susceptibility χ=-9.05 × 10^{-6}, while bulk water may have both diamagnetic (– 3 nT) and paramagnetic (about +1.5 nT) properties. Experimental results showed that under influence of oscillatory magnetic field with Larmor frequency water may be organized in clusters and change para/dia magnetic state.

Using spinner magnetometer and optomagnetic imaging spectroscopy techniques it has been shown that healthy tissues and unhealthy/cancer tissues have different para/diamagnetic properties. Since water may change its para/diamagnetic properties under influence of oscillatory magnetic field and presence of nanomaterials in solution, it means that water based nanomedicine is one of the future approach not only in diagnostics but also in therapy of peculiarity phenomena.

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 ISBN 978-86-7236-089-9

THE SCIENCE OF ENTREPRENEURSHIP

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Whether the research is funded through the private or public purse, at some point you may turn it into a business.

According to Bloomberg, 8 out of 10 businesses fail in the first 18 months. In my experience of working with over 100 startups this may even be as little as 12 months depending on the start point you choose. It is worth noting that this time to fail does not include the many years of research before starting the business.

Business is about managing risk and where there is risk there is bound to be failure. It is not surprising therefore that businesses fail. Indeed failure can be a virtue depending on how one deals with it and what one learns from it. Nonetheless with high financial and psychological consequences of failure and the opportunity cost, a failure rate of 80% leaves plenty of room for improvement.

Although there are many reasons businesses fail there are some recurring themes or traps that we will explore in the presentation. The main trap is a consequence of not appreciating that 'people buy painkillers and not vitamins', i.e. failing to fully understand and communicate the "value proposition". Even once companies have understood this, they may then fall into the second trap of 'premature scaling' in attempting to grow their business without having a proven scalable business model. Millions may be spent and individuals blamed before the business finally closes.

How then do we increase the chances of success of our businesses? As scientists we already know the 'how', we have been using the method for hundreds of years. The scientific method. During the presentation we will see how it can be applied to growing a business by removing cognitive biases and testing market opportunity to uncover unmet pent-up demand. We will also see what investors will look for when you pitch to them, that your business has a genuine chance of success with strong barriers to entry led by team that is capable of exquisite execution.

ISBN 978-86-7236-089-9

pH DEPENDENT ANTIBACTERIAL ACTIVITY OF DEXTRAN-COATED NANOCERIA

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Cerium oxide (nanoceria) nanoparticles as a new platform possess antioxidant activity at physiological pH values. It plays a role as a protective agent for living systems against radiation damage, oxidative stress, and inflammation due to its capability to transition from Ce^{+3} to Ce^{+4} [1-2]. In addition to its protective properties, it is a free radical scavenger, which allows its use as a therapeutic agent to fight against cancer and other diseases due to a reduction in reactive oxygen species (ROS) [2-3]. Despite the promise of nanoceria as a therapeutic agent for cancer applications, it has not been extensively studied for antibacterial activity. Thus, in the current study, the antibacterial activity of dextran-coated nanoceria was examined against *Pseudomonas aeruginosa* (as a gram-negative bacteria) and *Staphylococcus epidermidis* (as a gram-positive bacteria) in terms of a dose, time and pH dependent manner. First, synthesized nanoparticles were characterized in terms of their size via Transmission Electron Microscopy (TEM). Following, antimicrobial activity of ceria nanoparticles was examined. We found that dextran-coated nanoceria was much more effective at killing *P. aeruginosa* and *S. epidermidis* at basic pH (pH=9) compared to acidic and physiological pH values (pH=5, pH=6, pH=7, pH=8). At pH 9, there was no growth when 500 μg/mL dextran-coated ceria nanoparticles were exposed to *S. epidermidis* and *P. aeruginosa* for 24 hours and 10 hours, respectively. At pH 6, there was a 1 to 2 hour time shift for lag-phase when 1000 and 500 μg/mL dextran-coated ceria nanoparticles were exposed to *S. epidermidis* and *P. aeruginosa*, respectively. No growth inhibition was observed at pH=7 and pH=8 in the case of the two bacteria species at all nanoceria concentrations. In summary, pH=9 is the most effective pH for nanoceria to obtain critical antibacterial activity. This study provides antimicrobial activity of ceria nanoparticles and their possible applications in different fields.

 ISBN 978-86-7236-089-9

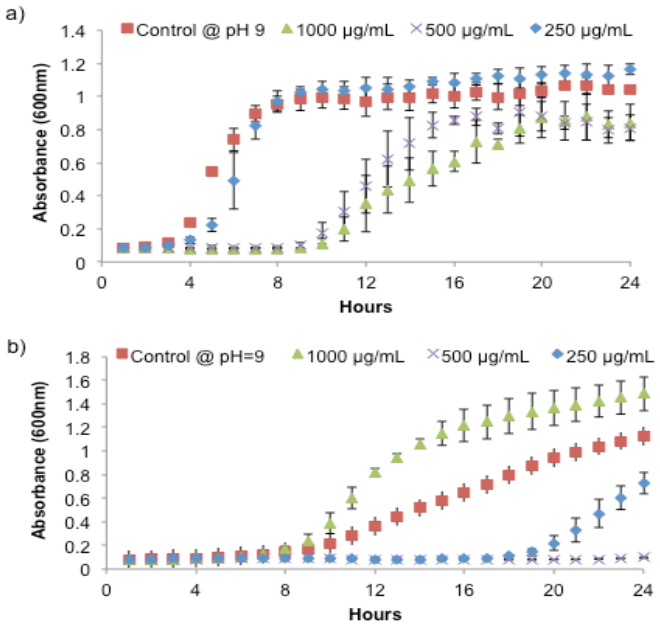

Figure 1: a) *P. aeruginosa* b) *S. epidermidis* were treated with 250, 500 and 1000 µg/mL at pH=9.

Keywords: Nanoceria, antimicrobial activity, reactive oxygen species

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Acknowledgements: Dr. Hilal Yazici is supported by TÜBİTAK–BİDEB, International Postdoctoral Research Scholarship Programme (Programme Number: 2219). The authors also thank Northeastern University for funding.

 ISBN 978-86-7236-089-9

THE POLYMERIC THERMOELECTRIC ENERGY HARVESTING SYSTEMS FOR BIOMEDICAL APPLICATIONS IODINE-DOPED MEH-PPV BLENDS WITH CARBON NANOTUBES

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Some of implantable medical devices require a battery to operate and this can represent a severe restriction. In most cases, the longevity of the whole implantable medical device is determined by the battery lifespan. For this reason, researchers have been studying energy harvesting techniques from the human body in order to obtain self-sustainable implantable medical devices. The main human-body energy sources are kinetic energy and thermal energy (1). This paper presents a potential thermoelectric polymeric energy harvester material for powering implantable medical devices. As they must be implanted, energy harvesting devices must be limited in size typically about 1 cm^3 -- and should provide available power between 6 nW and 7.2 mW (2).

This work aims to develop organic polymer based thermoelectric (TE) materials and to explore possibilities of biomedical applications of these materials. Based on previous research (3) we prepared drop cast films of commercially available poly [2-methoxy-5-(2-ethylhexyloxy)-1,4-phenylenevinylene] (MEH-PPV) with single walled carbon nanotube (SWCNT). The effects of solvent and molecular weight on the thermoelectric performance of nondoped and I_2 doped samples were investigated as a function of SWCNT concentration (0-50 wt %). The samples fabricated with the same molecular weight in a non-aromatic halogenated solvent showed higher power factors with an increasing trend for higher loads of SWCNT. In addition, samples made from high molecular weight polymer gave higher TE power factors by 3-4 fold than those of low molecular weight polymer based samples that were fabricated under the same experimental conditions. Moreover, the electrical conductivity of the samples in all variable conditions gave an increasing trend with elevated concentration of SWCNT, even before doping with iodine. However, Seebeck coefficients showed a decreasing trend with increased concentration of SWCNT in all conditions. Also, Seebeck coefficients of the samples made from low molecular weight polymer were slightly higher than those of high molecular weight polymer.

Keywords: thermoelectric, implantable medical, Poly [2-methoxy-5-(2-ethylhexyloxy)-1,4-phenylenevinylene], SWCNT

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 ISBN 978-86-7236-089-9

NANOHYBRID MAGNETIC MATERIALS FOR BIOMEDICAL APPLICATION

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Core-shell magnetic nanoparticles have received significant attention recently and are actively investigated owing to their large potential for a variety of applications. Gold-coated magnetic nanoparticles are a class of nanoparticles that have attracted much attention because of their advantageous characteristics, such as their inertness, non-toxicity, super magneticity, ease of detection in the human body, a magnetic core that is protected against oxidation, their facilitated bio-conjugating ability, catalytic surface, and their potential for a variety of biological applications. Gold-coated nanoparticles have great biocompatibility with the human body with the ability to interact with biomolecules such as polypeptides, DNA, and polysaccharides.

Herein we report a synthetic procedure for the preparation of water-soluble Fe_3O_4@Au core-shell nanoparticles, simple protocol for their purification by exclusion chromatography and methof for functionalization of gold surface with a number of sulfur-containing ligands (L-cysteine, 3-mercaptopropionic acid, 11-mercaptoundecanoic acid, lipoid acid, HS-PEG-COOH, 2-aminoethane thiol, spiropyran and others). Finally, magnetic nanoparticles were functionalized by immobilization of chymotrypsin. These magnetic nanoparticles were characterized by transmission electron microscopy (TEM), FTIR, DLS and UV-Vis spectroscopy.

We describe a distinct effect of non-heating superlow-frequency magnetic fields on the kinetics of chemical reactions catalyzed by the enzymes ⍵-chymotrypsin (ChT) immobilized on core-shell nanoparticles.

The observation is unprecedented and suggests the significance of magneto-mechanochemical effects induced by realignment of MNP magnetic moments in an AC magnetic field rather than traditional heating. Such low frequency and amplitude fields are safe and are not expected to cause any damage to biological tissues.

ISBN 978-86-7236-089-9

RAPID BONE REGENERATION WITH NANO-HYDROXYAPATITE COATED WITH A CHITOSAN-POLY (D, L)-LACTIDE-CO-GLYCOLIDE BONE-FILLING MATERIAL WITH OSTEOCONDACTIVE AND ANTIMICROBIAL PROPERTIES

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Composite biomaterials based on nano-hydroxyapatite have an enormous potential for natural bone tissue reparation, filling and augmentation. Multifunctional nanoparticulate systems based on HAp coated with biocompatible and bioresorbable polymers make a separate group of filler systems in bone tissue engineering [1,2]. Chitosan has many physicochemical (reactive OH and NH_2 groups) and biological (biocompatible, biodegradable) properties that make it an attractive material for use in bone tissue engineering. However, chitosan may induce thrombosis and it is therefore unsuitable as blood – contacting biomaterial. One of the strategies to improve the biocompatibility of chitosan is combination of this biopolymer with compounds that exhibit complementary properties.

In our studies, we present the synthesis, characterization, *in vitro* and *in vivo* research of a particulate form of nano HAp-coated polymer systems. We synthesized nanoparticulate HAp coated with chitosan (Ch) and a chitosan-poly-D,L-lactide-co-glycolide (Ch-PLGA) polymer blend obtained via the solvent/non-solvent method and freeze-drying processing. We also examined the possibility of using Thermo-Gravimetric Analysis/Differential-Thermal Analysis (DTA/TGA) coupled on-line with mass spectrometry (MS) as a *finger print* for identification purposes in coating processes. The quantitative antimicrobial test has shown that HAp/Ch-PLGA have some antibacterial properties (MIC (mg/mL): *Pseudomonas aeruginosa* – 6.40, *Staphylococcus aureus* – 6.40, *Staphylococcus epidermidis* – 3.20). MTT assay was used to test cytotoxicity and cell viability. By using HAp/Ch-PLGA in the form of a filler a high level of reparatory ability, with the presence Haversian canals and cement lines in reconstructed of bone defect, was achieved *in vivo*.

Key words: nano-hydroxyapatite, chitosan, poly(DL-lactide-co-glycolide), bone-filling material

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 ISBN 978-86-7236-089-9

AQUAPHOTOMIC STUDY OF HYDRATED HYDROXYLATED FULLERENE BASED ON SKIN NANOCREAM: WATER BASED NANOMEDICINE

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Water is one of the major constituents of skin, and its role is of vital importance for skin barrier function. Many problems and diseases of the skin involve water organization in skin either as a cause or the consequence. Therefore, the specially engineered skin cream formula based on nanomaterial which can organize water molecules around it can have beneficial effects on skin. In this study near infrared spectroscopy was used to find out how the water molecules are organized around a certain type of hydrated hydroxylated fullerene, so called nanoharmonized substance - NHS. The first part of the present study was aimed at discovering how the water molecules are organized in water solutions with different concentrations of NHS. The second part of the study was aimed at characterizing emulsion and Nanocream in NIR region, and discovering how the NHS in Nanocream will react to added water. In the last part of the study, effects of created Nanocream on the skin of three human volunteers were assessed during the course of 8 days. The results of the study are presented and discussed in accordance with the method of Aquaphotomics, a specific water-mirror approach, which is able to recognize changes in molecular conformations of the water matrix and thus reflect specific perturbations caused by the present nanomaterial.

Keywords: hydrogenated hydroxylated fullerene, water, skin hydration, anti-oxidants, near infrared, Aquaphotomics

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 ISBN 978-86-7236-089-9

STEM CELLS FROM FAT TISSUE AND THEIR APPLICATION - PILOT STUDY IN PATIENTS WITH ANAL FISSURES

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An anal fissure is one of the most common anorectal diseases, a chronic non-infectious condition which impairs the quality of life, mostly due to often severe pain during or after defecation. It occurs most frequently in young adults. Men and women are equally affected. We treated 6 patients age between 20-50 years old, with chronic fissure (more than 6 weeks) that didn't respond to conventional conservative therapy and were candidates for lateral internal sphincterectomy. Exclusion criteria were: autoimmune diseases, presence of malignant or chronic infectious disease, or on immunosuppressive therapy. Before the procedure all routine preoperative tests were done. Patients were asked to quantify their pain using VAS scale of pain before and on each consultation after the procedure. Under local anaesthesia and sedation, lipoaspiration of approximately 150mL of fat tissue from the abdominal area was done. Adipose derived regenerative cells (ADRCs) were extracted using Celution 800/CRS device and were reinjected directly in the fissure and as enriched fat graft in subcutaneous layer underneath the fissure. The average number of cells reinjected was $3{,}20 \times 10^7$. The patients were followed up after 1 week, 1, 2, 3 and 4 months after the procedure. Significant improvements in local symptoms were achieved in all cases. Detail analyse of each case is given. Application of ADRCs is the method of great potential when considering chronical wounds including anal fissures. The results of similar studies showed its efficacy in treatment of anal fistulas and significant improvement in sphincter incontinence when combined with traditional surgical treatment. Further studies have to be done to obtain more accurate data, but we strongly believe that the stem cells will fulfil a clear unmet medical need and will help improve the healing and hence the quality of life of patients with anal fistula, fissure and sphincter dysfunction.

Key words: anal fissures, ADRCs, stem cells

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 ISBN 978-86-7236-089-9

DEVELOPMENT OF PEGYLATED PLGA NANOPARTICLE FOR CONTROLLED AND SUSTAINED DRUG DELIVERY IN CHRONIC MYELOID LEUKEMIA

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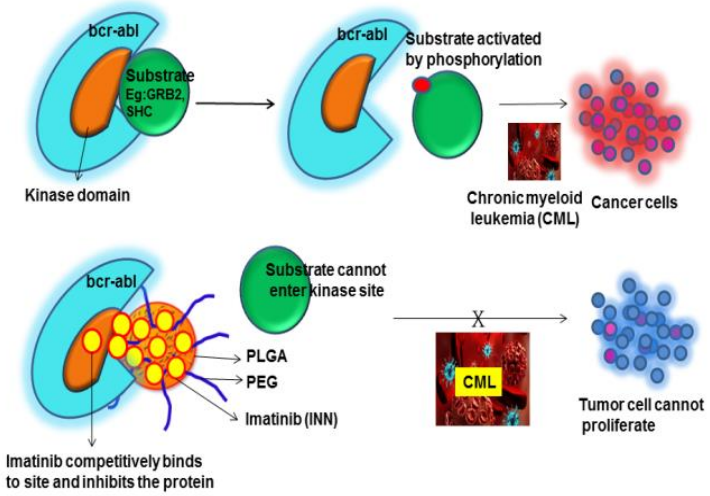
Imatinibmesylate (INN) is an anticancer agent used in the treatment of chronic myeloid leukemia (CML), gastrointestinal stromal tumours (GIST) and other related diseases which involve deregulated tyrosine kinase activity [1, 2]. This promising drug(Gleevec or Glivec), approved by the U.S. Food and Drug Administration in 2001, was designated as a "magic bullet" and was recognized for its capacity to deal with fatal cancers converting them into manageable chronic conditions[3]. Currently available non-nanoparticulate Imatinibmesylate dosage forms have disadvantages like variable systemic availability, development of resistance on long term due to activation of efflux transport system, poor brain penetration, and side effects including oedema, local gastric irritation, dyspepsia, skin rashes, muscular cramps, most of which are dose dependent. The objective of this work is to develop a nanoparticulate drug delivery system of INN using a biodegradable polymer such as m-PEG-PLGA di-block copolymer. The design of Imatinibmesylate nanoparticles is proposed for better bioavailability by prolonged systemic circulation and effective drug delivery at the site of action with a controlled release. A series of biodegradable monomethoxypoly (ethylene glycol)-poly (lactic-co-glycolic) acid (m-PEG-PLGA) copolymers were synthesized in the present investigation. Synthesis and characterization of monomethoxypoly (ethylene glycol)-poly (lactic-co-glycolic) acid (m-PEG-PLGA) nanoparticles to encapsulate INN by an emulsion solvent evaporation method, creating a pH dependent, hydrophilic INN/m-PEG-PLGA nanoparticles has been achieved. The Nps had a mean particle size of<200nm, spherical in shape, encapsulation efficiency of 80%and prolonged drug release behavior.



Schematic representation of imatinib released from mPEG-PLGA NPs inhibiting CML

Keywords: Imatinib, Leukemia, Poly (lactic-co-glycolic) acid, Poly (ethylene glycol), Drug delivery

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 ISBN 978-86-7236-089-9

RAMAN & FLUORESCENCE-BASED MULTIPLEXED REALTIME IMAGING

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Optical-based endoscopic imaging techniques have drawn interests in *in vivo* diagnosis owing to its accessibility to internal tissue and real time detection. However, conventional white light-based endoscopy can only offer morphological information without other information to clearly identify the subtle change in flat and suspicious lesions. [1] In order to improve information of endoscopic diagnosis, many attempts to combine the additional functionality with endoscopy such as bioluminescence, fluorescence, and Raman scattering have been tried. [2-4].

In this study, we illustrate the fluorescence-Raman (dual modal) endoscopic system (FRES) for *in vivo* multiplexed molecular diagnostics utilizing fluorescence & SERS active nanoprobes (F-SERS dots) which can simultaneously give fluorescence and Raman signal. [5] This dual modal endoscopic system exhibits high sensitivity and multiplexing capability for *in vivo* endoscopic molecular diagnostics with the following imaging and targeting strategies: I) simultaneous detection of dual modalities (fluorescence and Raman scattering) for fast imaging of target with fluorescence signal and identification of multiple targets with Raman signals, ii) utilization of F-SERS dots as tumour-targeting agents via direct topical administration method, and iii) provision of real-time multiple-target endoscopic imaging using optical fibre bundle for intraoperative molecular diagnosis. Sensitivity of FRES characterized with tumour-targeting agents in conical tube was high enough to detect 1-pM of F-SERS dots. The human epidermal growth factor receptor 2 (HER2) and epidermal growth factor receptor (EGFR) were successfully recognized on the breast cancer xenograft mouse, illustrating that FRES has significant potential as a clinical molecular diagnosis tool that can be utilized during routine endoscopic procedures.

Keywords: multiplex analysis system, Fluorescence-SERS dots, in vivo imaging, endoscope

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 ISBN 978-86-7236-089-9

SERS NANO PROBES FOR BIO APPLICATIONS

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Recently, SERS (surface-enhanced Raman scattering) technology has broadened the applications of Raman spectroscopy in biomedical analysis field. During the last decade, we have developed various multifunctional SERS tagging materials; SERS dots, F-SERS dots, M-SERS dots, and NIR SERS dots, which have many advantages; lack of photo-bleaching, narrow peak band width and single laser excitation is used for detection of multiple targets. They have been successfully utilized in screening and identifying biological molecules in vivo and in vitro system.

Through Pioneer Research Centre program at SNU, we have developed multiplex SERS analysis system to be used as a diagnostic reagent and for detecting disease such as cancer by combining SERS labelling, nano spectroscopy, bio-MEMS, and biomedical technologies. The multiplex analysis technology requires highly sensitive SERS nanoprobes which can give quantification analysis results. The multiplex analysis system can be applied to develop diagnostic reagents, especially antibodies, and disease diagnosis technology. The current blood tests platforms in hospital can be replaced by the multiplex analysis system using SERS dots, resulting in reducing sample consumption and enhancing the testing efficiency. For this, several platform technologies have been developed, which ultimately can be used for disease monitoring system, such as in vitro cancer diagnosis, in vivo imaging, and point-of-care-testing (POCT), which will become a core technology for ubiquitous health care system in a near future.

Keywords: multiplex analysis system, SERS dots, in vivo imaging, point-of-care-testing

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 ISBN 978-86-7236-089-9

INVESTIGATION OF THE HEV BLUE LIGHT BLOCKING EFFECT OF NANOPHOTONIC MATERIAL

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This research is motivated by harmful effect of the artificial lightning that has extreme peak in high energy visible (HEV) blue light band that has a short wavelength from 450 to 495 nm [1]. Human eye is adapted to sunlight by evolution. However the prolonged exposing to video display terminals, televisions, personal computers smart phones and tablets leads to consequences of age related degeneration of eye inner structures. For 90% of people, who spend more than 3h per day in front of aforementioned digital devices, this is known as computer vision syndrome. We incorporate fullerol $C_{60}(OH)_{24}$ into existing ophthalmic polymer based on PMMA and produce new nanophotonic material that block HEV blue light up to 70% (Fig 1). The investigation of phototoxicity effects was done with VIS/NIR spectrometers (Hamamatsu, Japan) connected to the monochromator ranging from 350 nm to 850 nm (Optometrics, USA). From the presented results [2] of the transmittance of nanophotonic and reference materials, it can be concluded that the new nanophotonic material show lower transmittance of HEV blue light than reference material. Since the new nanophotonic material significantly block up harmful light, it could be suitable for the PMMA-based lighting products, displays and ophthalmic application that including RGP contact lenses. Nanophotonic contact lenses show high potential to become optical devices necessary for the healthy life style providing overall protection from HEV blue light.

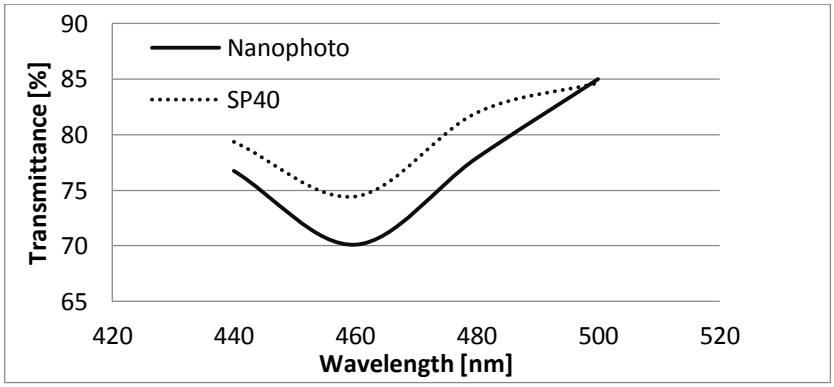

Figure 1. Transmittance for nanophotonic and reference contact lens material

Key words: Phototoxicity, Nanophotonic opthalmic materials, Transmissivity, Blue light

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 ISBN 978-86-7236-089-9

CHARACTERISATION OF PHOTONIC NANOMATERIALS FOR CONTACT LENSES, BEFORE AND AFTER EXPOSURE TO EXTERNAL MAGNETIC FIELD BY SPINNER MAGNETOMETER AND OPTOMAGNETIC IMAGING SPECTROSCOPY

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Poor solubility of fullerene C_{60} often makes it inappropriate for applications therefore its incorporation into polymers provides new materials which can be processed. These materials' properties are a combination of unique fullerene C_{60} properties and specific properties of a polymer. The development of chemical reactions able to modify the chemical structure of C_{60} led to new fullerene derivatives with outstanding structural, magnetic, superconducting, and electrochemical and photophysical properties [1]. The problem of low solubility of fullerene is surpassed by its functionalization with –OH groups making a new molecule called fullerol $C_{60}(OH)_{24}$. The photonic nanomaterials are synthesized by incorporating fullerol $C_{60}(OH)_{24}$ into commercial soft contact lens material Definitive74 made by Contamac, UK. Three different mass concentrations of fullerol are used: 0.003%, 0.01% and 0.015%. Hence, three materials for soft contact lenses are produced and the fourth material, the standard one, was used as a reference sample. The purpose of incorporating fullerol into polymer was to develop new materials for soft contact lenses with improved optical and mechanical characteristics. The magnetic properties of polymers change due to fullerol presence therefore the aim was to show the differences in magnetic properties of the materials before and after the exposure to two different external influences. The first one is the influence of a human being and the second one is the Bioptron® lamp [2]. The measurements of a remanent magnetization of these materials are done by spinner magnetometer, JR-6A. These results were compared with the results acquired by Opto-magnetic imaging spectroscopy (OMIS) [3].

Keywords: soft contact lenses, fullerene, spinner magnetometer, remanent magnetization

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 ISBN 978-86-7236-089-9

LONG-TERM OUTCOMES IN POPULATION UNDERGOING PLASMONIC PHOTOTHERMAL THERAPY OF ATHEROSCLEROSIS WITH SILICA-GOLD NANOPARTICLES: SAFETY IN NANOM-FIM TRIAL

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Introduction: Our previous bench studies PLASMONICS[1] and NANOM First-in-Man (FIM) trial[2, 3] documented total atheroma volume (TAV) reduction up to unprecedented 79.4 and 60.3 mm^3 respectively. Moreover the concept was partly validated in another experiments[4]. But the safety options in nanomedicine raise an issue of the optimal niche of these technologies at the real-world clinical practice.

Methods: This is a retrospective analysis of the 5-year long-term clinical outcomes at the intention-to-treat population (n=180) of NANOM-FIM trial (NCT01270139). The primary outcome was a composite of end-point of MACE-free survival, MACE, cardiac death, TLR (target lesion revascularization) and TVR (target vessel revascularization).

Results: Mortality (6 vs 9 vs 10 cases of cardiac death in groups respectively, $p<0.05$), MACE (14.3% of nano group vs 22.9% in stenting control, $p=0.04$), late thrombosis (2 vs 4 vs 6 cases in groups respectively, $p<0.05$) and TLR (3.8 vs 5.7% in nano and stent group respectively, $p=0.04$) were significantly higher in ferro group and stent control at 60-month follow-up (fig. 1), but the difference in the proportion of MACE-free survival and TVR incidence when compared between groups did not reach statistical significance ($p=0.33$). Diabetes ($p=0.03$), hypertension ($p=0.05$), previous or simultaneous PCI ($p=0.048$) and heart failure ($p=0.04$) were confirmed as strong independent predictors of cardiac death with high rate of mortality and late thrombosis in patients underwent stenting.

Conclusion: NANOM-FIM trial demonstrates high safety of the selected nano-technologies with better rate of mortality, MACE and TLR at the long-term follow-up if compare with conventional implantation of the second generation stent XIENCE V.

 ISBN 978-86-7236-089-9

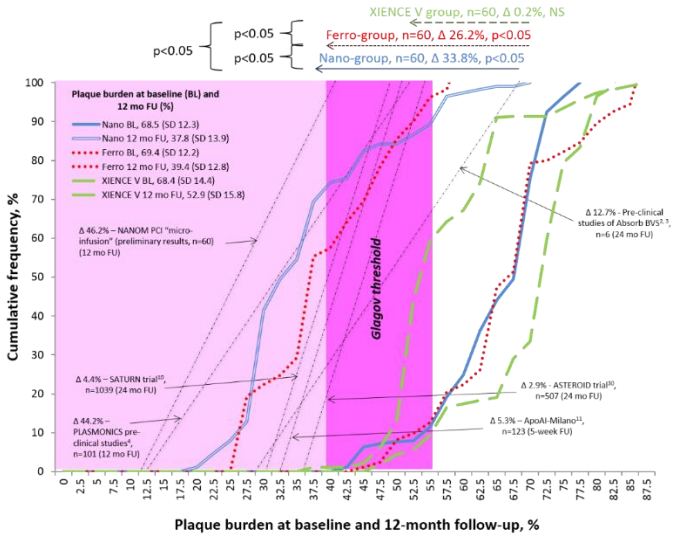

Figure 1. Cumulative frequency of plaque burden at baseline and 12-month follow-up.

A panel depicts curves of cumulative frequency of plaque burden (%) at baseline and 12-month follow-up at three groups in comparison with historical data of the pre-clinical and clinical ABSORB, ASTEROID SATURN, and ApoAI-Milano[3] studies with documented alterations in plaque burden. At the top of the figure the main statistical changes in plaque burden at NANOM-FIM trial are described. The hot pink zone shows so called *Glagov threshold* of a 40-55% plaque burden. The light pink zone performs an area of athreroregression below "true" 40% *Glagov threshold*.

Key-words: atheroregression, nanomedicine, plasmonics, safety, long-term outcomes.

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ISBN 978-86-7236-089-9

REMANENT MAGNETISM ON NANO AND PICO TESLA LEVEL OF BIOLOGICAL TISSUES

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Bio-magneto-chemistry is the study of states and interaction of ions and charged molecules in biological tissues. When the ions or charged molecules are not in interaction, then the tissue phenomena may be explained by paramagnetism. However, when ions and charged molecules are in interaction, it cause collective phenomena and tissue properties has a dynamical paramagnetic/diamagnetic values.

In our research three major substances and tissues are investigate: water, blood and colon tissues. Water is playing important role in biological tissue, because it consists of ions like Na^+, K^+, Ca^+, Cl^- etc. having magnetic susceptibility per gram atom (10^6 emu) of -6.8, 14.9, -10.4, -23.4, respectively. Bearing in mind that human body content 60 -75% water (depending on age) its importance for bio-magneto-chemistry turns to be significant. Single water molecule is diamagnetic (magnetic susceptibility per gram atom is -13×10^{-6} emu) but in bulk state could be both paramagnetic +1.5 nT and diamagnetic -2.5 nT. Second important substance for bio-magneto-chemistry is blood, which contents iron (Fe^{2+}) in haemoglobin and is responsible for oxygen (O_2) transport. Both Fe^{2+} and O_2 are strong paramagnetic, but when linked together their complex appear week paramagnetic (0.15 nT) or diamagnetic properties.

In this report colon tissues, healthy and unhealthy (cancer), are presented. To measure magnetic properties of colon tissues dual spinner magnetometer JR6A (AGICO s.r.o.) with accuracy of 3pT (±2,4 μA/m) is used. The results show clear differences between healthy tissue and cancer with average values of 1.82 nT (1.452557±0.072 mA/m) for healthy tissue and 0.42 nT (0.33438 ± 0.018 mA/m) for cancer. Results obtain with JR6A dual spinner magnetometer were compared with other method called Opto-magnetic imaging spectroscopy. Histograms of colon cancer showed different wavelength difference and intensity of characteristic peaks obtained by OMIS method (average values of the activity in the domain of +8,96 n.a.u. in paramagnetic zone and -5,22 n.a.u. in diamagnetic zone for characteristic peaks and wavelength difference from 105 nm until 185 nm). It can be concluded that gap between healthy and cancer tissue strongly suggests that nano/pico-magnetophysics might be a method for tissue state characterization.

Key words: nanophysics, colon, cancer, paramagnetism, diamagnetism

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 ISBN 978-86-7236-089-9

WATER STRUCTURED BY VERY LOW CONCENTRATIONS OF FULLEROL: IMPLICATIONS FOR DOMINANT ROLE OF WATER IN THEIR ANTIOXIDANT AND RADIOPROTECTIVE EFFECTS

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Fullerene compounds are known to possess antioxidant properties, a common property of chemical radioprotectors. It is recently hypothesized that the antiradical action of hydrated fullerenes in water medium is due to a hydrated free radical recombination catalyzed by specific water structures, and not a result of direct binding to double bonds of fullerene core. This hypothesis was only logical explanation for the peculiar results of OH-removing efficacy in reverse correlation with fullerene concentration. [1] The proposed model of antiradical activity corresponds with the model of exclusion zone water formed next to charged surfaces or so called liquid crystalline water. [2]

Fullerols – water-soluble fullerene derivate, being hydrophilic and highly electronegative have basic properties of surfaces for exclusion zone water formation. However, exclusion zone water spectral features are not yet defined for nanostructures because appropriate methods are lacking.

To determine whether fullerol creates exclusion zone water, a newly developed framework for analysis of water near infrared spectra in the region of 1st overtone of water called Aquaphotomics [3], was applied. Using the aqueous fullerol solutions serially diluted in concentrations ranging from 1.128mg/ml to 15.625ng/ml it was found that near infrared spectra of aqueous solutions with ultra-low concentrations of fullerol had the same spectral features observed in near infrared spectra of water next to Nafion – a known and potent exclusion zone creator.

These common spectral features for exclusion zone water and highly diluted fullerol solutions correspond to strong hydrogen-bonded large water molecular structures (region from 1447 to 1518 nm). These findings confirm the hypothesis of exclusion zone formation around fullerols in aqueous media and suggest dominant role of water in their antioxidant activity.

Keywords: fullerene, water, aquaphotomics, exclusion zone water, hydrogen bonds

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 ISBN 978-86-7236-089-9

DEVELOPMENT OF MOISTURISING SKIN CARE PRODUCT WITH NanoHS

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Nano-harmonized substance (NanoHS) is patented, safe and efficient active ingredient for medical and cosmetic application. It is made by modifications of fullerene molecules, first by functionalization of the C_{60} molecule with OH groups (C60(OH)x) and second, through the addition of OH groups by water layers, (wNHS) C60(OH)x@(H2O)y (Fig.1). These water layers (yellow markings), protects the C_{60}(OH)x complex from environmental influences, and at the same time, they isolate fullerene structure, prevents any toxicity of C_{60}, but keeps all beneficial effects for the biomolecules. This structure has diameter size between 4,7-9,5 nm and it is water soluble and simple to formulate. In last decades, functionalized fullerenes is used in personal care products, mostly as a free radical-scavenger, in moisturizing face creams, sunscreens, in whitening, antiaging, and cellulite control preparations.

We formulate the base cream (emulsion o/w), base cream with hyaluronic acid, ceramide or NMF-like commercial combination of substances, in amounts suggested by the producer for each ingredient. In all of these formulations, we incorporate nano-HS (1%). The aims of this work were to investigate the mutual compatibility of nano-HS and these ingredients and possible influences of nano-HS on their moisturizing properties in skin care products. To characterize the properties of these products, we used FTIR and opto-magnetic image spectroscopy (OMIS). Differences in short time improvement of moisture content in the skin we examined by bioimpedance measurement of skin volunteers. Results of these investigations enabled us to develop the further formulation.

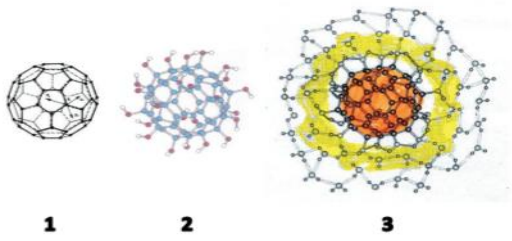

Figure 1: modifications from fullerene molecules (1) trough fullerols (2) to nano-harmonised substance nanoHS, (3), US Patent 8,058,483 B2 , 2011

Key words: functionalized fullerenes, skin care, moisturisation, FTIR, OMIS, bioimpedance

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 ISBN 978-86-7236-089-9

BIOPHYSICS OF PAIN SUPPRESSION BY POLARIZED LIGHT AND NEAR INFRARED IRRADIATION: EXPOSURE OF ACUPUNCTURE POINTS ON NANO SCALE

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BACKGROUND. According to clinical studies acupuncture is an effective method for many pain syndromes treatment. But there are no experimental proofs that exposure of acupuncture points to low intensity incoherent polarized light evokes an analgesic affect.

OBJECTIVES. Our previous work show that exposure of acupuncture points of mice to low intensity microwaves effectively weakens the pain. The purpose of this study was to determine whether exposure of acupuncture points to low intensity incoherent polarized light evokes a statistically significant pain reduction.

METHODS. We studied BIOPTRON device polarized light influence (480-3400 nm, polarization - 95%, noncoherent, 40 mW/cm^2 – PILER-light). We tested the effects of PILER- light on acute (the threshold of vocalization during electrical stimulation of the foot) and tonic (the duration of licking of formalin injected paw) pain behavioral responses in mice. Measurements were done before and after exposure on analgesic acupuncture points E-36, V-56 and V-60 or on the skin that did not contain them.

RESULTS. Exposure of acupuncture points to polarized light evoked a statistically significant increase (by 34.2-59.1%) of pain threshold and shortening (by 32.3 –50%) of licking time in mice. The most effective acupuncture point was E-36 both the painful and the normal paw. After 2 min, 6 min and 10 min exposure to PILER-light, analgesia was 7.6%, 30.9% and 50%, respectively. The exposure to PILER-light on a skin that did not contain analgesic acupuncture points did not evoke significant effect.

CONCLUSIONS. The results show the efficacy of pain suppression by exposure of antinociceptive acupuncture points to PILER-light. We assume that better effects appear from biophysical interaction of polarized light and biological structures in acupuncture points on a nano scale. This analysis will be presented in paper.

Key words: polarized light; acupuncture points; acute pain; tonic pain; behavioral responses; analgesia.

 ISBN 978-86-7236-089-9

MgO NANOMATERIALS IMPROVE CELL FUNCTIONS AND REDUCE BACTERIAL INFECTIONS FOR ORTHOPEDIC TISSUE ENGINEERING APPLICATIONS

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Regeneration of complex orthopaedic tissues (such as ligaments, bones, and the tendon-to-bone insertion site) is problematic due to a lack of suitable biomaterials with the appropriate chemical and mechanical properties to elicit formation of tissues with similar structure, organization, and functionality to natural tissues. Additionally, a non-trivial fraction of implanted biomaterials contract bacterial infections, which can lead to implant failure, secondary surgeries, and the spread of infection to other tissues throughout the body. To address these issues, the current study investigated magnesium oxide (MgO) nanoparticles as novel materials to improve orthopaedic tissue regeneration and reduce bacterial infection.

Here, MgO nanoparticles and hydroxyapatite (HA) nanoparticles were dispersed within poly-L-lactic acid (PLLA), and the resulting nanocomposites were tested for their mechanical properties, surface roughness, degradation characteristics, antibacterial properties, and their ability to support the adhesion and proliferation of fibroblasts and osteoblasts.

Results showed for the first time that nanocomposites containing both HA and MgO nanoparticles performed best with respect to osteoblast proliferation and mechanical properties. Increases in alkaline phosphatase expression and vinculin focal adhesions within osteoblasts indicated the ability of MgO to enhance the osteogenic properties of HA composites. Further, varying MgO concentrations offered tunable composite degradation kinetics, and the supernatant from degraded composites containing MgO nanoparticles supported greater osteoblast proliferation compared to non-MgO composites. Bacterial experiments with *Staphylococcus aureus* showed that MgO nanoparticles exhibit powerful bactericidal efficacy, suggesting that MgO nanoparticles should be incorporated into scaffolds for orthopaedic tissue engineering to improve cell functions and reduce the risk of bacterial infection with limited antibiotics usage.

Keywords: MgO; nanomaterials; tissue engineering; orthopaedic; antibacterial

 ISBN 978-86-7236-089-9

SILVER NANOPARTICLE-EMBEDDED POLYMERSOME NANOCARRIERS FOR THE TREATMENT OF ANTIBIOTIC-RESISTANT INFECTIONS

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Antibiotics have been extensively used since their commercialization to treat patients suffering from a wide variety of infectious diseases. When utilized correctly, these drugs are extremely effective at reducing mortality rates and healing time, which makes them essential in the clinic today. Unfortunately, however, antibiotics have been used so prevalently over the last 80 years that the bacteria they were designed to kill have begun to evolve and adapt, rendering these drugs ineffective. According to the Centre for Disease Control's 2013 report on antibiotic resistance in the United States, at least 2 million people acquire serious infections from antibiotic resistant bacteria each year, and over 23,000 die as a direct result.

This study explored the development and optimization of a polymersome nanocarrier formed from a biodegradable diblock copolymer to overcome bacterial antibiotic resistance. Here, polymersomes were synthesized containing silver nanoparticles embedded in the hydrophobic compartment, and ampicillin in the hydrophilic compartment. Results showed for the first time that these silver nanoparticle-embedded polymersomes (AgPs) inhibited the growth of *Escherichia coli* transformed with a gene for ampicillin resistance (bla) in a dose-dependent fashion. Free ampicillin, AgPs without ampicillin, and ampicillin polymersomes without silver nanoparticles had no effect on bacterial growth. The relationship between the silver nanoparticles and ampicillin was determined to be synergistic and produced complete growth inhibition at a silver-to-ampicillin ratio of 1:0.64. In this manner, this study introduces a novel nanomaterial that can effectively treat problematic, antibiotic-resistant infections in an improved capacity, which should be explored for a wide range of medical applications.

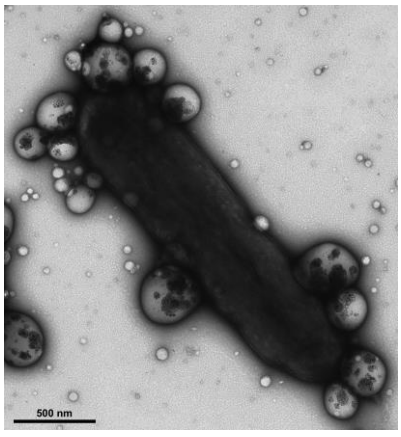

Figure 1. Cell-particle interactions were visualized via transmission electron microscopy. Images display the silver nanoparticle-embedded polymersomes aggregating around and sticking to an antibiotic-resistant *E. coli* bacteria

Keywords: antibiotic-resistance, polymersome, silver nanoparticle, nanomedicine, bacteria

 ISBN 978-86-7236-089-9

SELENIUM NANOPARTICLE COATINGS FOR ANTI-CANCER, ANTI-BACTERIAL BONE ENDOPROSTHESES

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Selenium is a trace element micronutrient that is associated with antioxidant and metabolic mechanisms in the body. Selenium nanoparticles (SeNP) have been demonstrated to effectively reduce both gram-positive (e.g., *S. aureus*) and gram-negative (e.g., *P. aeruginosa*) bacteria, while having a safe toxicity profile to healthy fibroblasts and osteoblasts. Here, we describe the synthesis, characterization and efficacies of different selenium nanoparticle (SeNP) formulations, both as suspensions in solution and as nanocomposites within poly (l-lactic acid) (PLLA) films for changes in cytotoxicity, bone cell activity (both cancerous and non-cancerous) as well as prevention of infection establishment. To ensure precise and consistent SeNP coverage, we aim to tabulate several relevant aspects of the particle. By adjusting the parameters of the reaction producing SeNP, a variety of data can be collected and analysed. Characteristics that are pertinent include the nanoparticle size and coverage, which in turn affects the surface roughness and chemical reactivity. Thus, a cubic response surface model has been developed using a central composite design (CCD), to predict the SeNP coating and the resulting effect on cellular interactions. Nano-scale roughness is known to modify protein adsorption (and thus cellular response) onto the surface of a material. With this CCD model, we can predict the changes in SeNP coverage according to our synthesis parameters, and better direct the cell-material interactions that result. We have seen decreases in bacterial adherence, proliferation and deposition of biofilm while at the same time improving healthy mammalian cell growth on these SeNP surfaces.

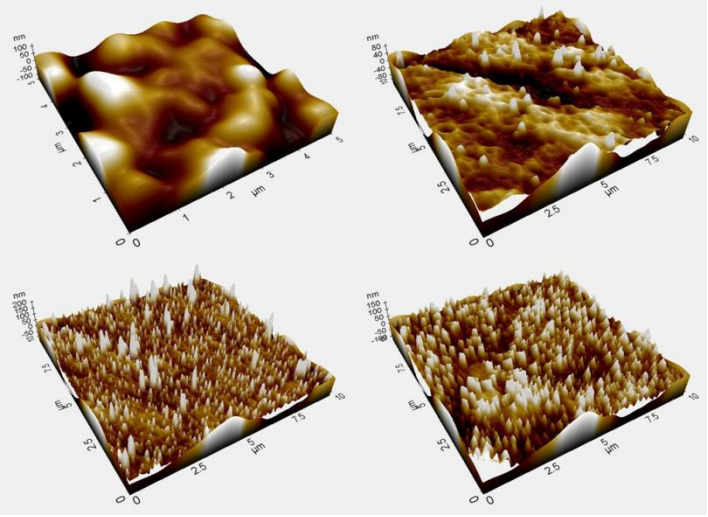

Figure 1. Atomic force microscopy surfaces of PLLA treated with 30 seconds of glutathione and sodium selenite followed by 0, 5, 30 or 60 seconds of exposure to NaOH, clockwise. Nanoroughness for all samples generally increased with longer development times (and thus greater SeNP coverage).

ISBN 978-86-7236-089-9

DRUG RELEASING IMPLANTS BASED ON NANOENGINEERED TITANIA NANOTUBES FOR LOCALIZED BONE AND CANCER THERAPY

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To address limitations of systemic drug delivery localized drug delivery systems (LDDS) based on nano-engineered drug-releasing implants are recognized as a promising alternative. Nanoengineered titania nanotubes (TNT), synthesized by simple self-ordering electrochemical process regarding to their many outstanding properties are emerged as one of the most important contenders for these applications. This work highlights the recent development of advanced LDDS based on TNTs by our group, focusing on strategies for controlling their drug release performances based on structural modification, altering their internal chemical functionalities, controlling pore openings by biopolymer coating and polymer micelles as nano-carriers used for multi-drug delivery and external stimulus drug release. Several new concepts and the application of TNTs wire drug-releasing implants for localized bone and cancer therapy are presented and discussed.

Key words: local drug delivery, drug-releasing implants, titania nanotubes

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 ISBN 978-86-7236-089-9

ULTRASTABLE SURFACTANT FREE METAL NANOPARTICLES STUDY FOR BIOMEDICAL APPLICATIONS

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Metallic nanoparticles (MNP) with diameter ranging from 2 to 100nm have received extensive attention during the past decades due to their high potential applications such as magnetic data storage, magnetic hyperthermia therapy, gene delivery for the magnetic nanoparticles, but also catalysis and cancer therapy for noble-metal nanoparticles.[1]

The main interest in MNP comes from their unique chemical and electronic properties due to their large surface-to-volume ratio.[2] The advances in preparing MNPs, specifically using sol-gel methods, have improved the MNP samples remarkably giving monodisperse nanoparticles with a good size and shape control and distribution during the synthesis. There is a need for a simple, reliable, surfactant free low cost method for producing homogeneous stable metal nanoparticles and we recently developed one that enables the production of surfactant free stable MNPs under air[3] . Their unusual stability in air allows applications previously difficult to implement with metal nanoparticles produced using conventional methods due to their pyrophoric properties.

This paper present the study of ultrastable metal nanoparticles (Ag and Co) aimed to be used for biomedical applications. X-ray diffraction measurements showed that MNPs are highly crystalline and stable at high temperature. Transmission Electron microscope micrographs revealed highly crystalline monodisperse nanoparticles and thermogravimetry analyses did not show any weight loss demonstrating the high purity of these MNPs. The biocidal properties of these MNPs were also study against bacteria and fungi. This study shows that these MNPs do not degrade with time and can be recycled after use. The functionalization and encapsulation of these MNPs will also be discussed.

To validate a potential use of these MNPs, their toxicity was also studied using Human Embryonic Kidney Cells (HEK 293), Hela cells and cancer cells. The effect of these nanoparticles on human cells will be discussed in terms of possible biomedical applications and cancer treatment.

Key words: Metal nanoparticles, biocidal properties, toxicity, cancer cells

Financial support from through the Estonian Research Council (grant number PUT431), Marie Curie (PERG05-GA-2009-249243) and the Estonian Road Map infrastructure and the NAMUR projects is acknowledged.

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 ISBN 978-86-7236-089-9

NANOPHYSICAL APPROACH OF ENDOCERVICAL AND EXOCERVICAL SMEARS CHARACTERIZATION USING OPTOMAGNETIC IMAGING SPECTROSCOPY

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Light-matter interaction of diffuse visible and reflected polarized light is the basis of Opto Magnetic Imaging Spectroscopy (OMIS). This novel nanophysical diagnostic technique identifies average energy state of valence electrons and hydrogen bonds within the sample material. Calculation based on valence electron velocity of matter gives the ratio between magnetic force (F_M) and electrical force (F_E) of matter $F_M/F_E \approx 10^{-4}$. Since force (F) is directly related to action ($A= F \times d \times t$, where F is force in range 0,01 – 1.0 nN, d is displacement in range 0,1 – 5.0 nm, and t is time in range 10^{-8}-10^{-10}s), it can be concluded (based on Planck constant/action of 6.626×10^{-34} Js), that the magnetic force of matter is four orders of magnitude closer to quantum state of matter than the electrical force. This opens an opportunity to detect the conformational states and changes in the matter at nano scale level using OMIS light-matter interaction method.

In our investigation nanophysical approach of light-matter interaction (OMIS) was used to characterise Papanicolaou (PAP) smears. The PAP test is still the most effective screening test for cervical cancer detection, despite its varying specificity and low sensitivity. In conventional cytology, cervical sample is smeared directly on microscopic slide and stained and inspected afterwards. In some countries, liquid based cytology has not been established yet and cervical cancer is diagnosed based on the microscopic evaluation of two slides containing cervical samples from the endocervix and exocervix separately. This doubles the time needed for test results and increases the cost of the test. Optomagnetic imaging spectroscopy is fast and accurate method for detecting abnormal changes in cervical cells. Based on 158 exocervical and 158 endocervical samples, classification accuracy of Optomagnetic imaging spectroscopy results achieved, using Naive Bayes classifier, is 85% for unstained exocervical samples and 80% for unstained endocervical samples. Benefits of OMIS used for endocervical and exocervical smears characterization are: (1) increased sensitivity and specificity, (2) time saving (results of the OMIS are provided within 10 min, while current time of waiting for results in the best case is 2-7 days), (3) cost reduction (there is no need for laboratory services, chemicals for staining, sample transport, and sample storage), and (4) reduced psychological pressure for women who have to wait for the screening results.

Keywords: nano physics, cervical cancer, optomagnetism, imaging spectroscopy, screening test

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 ISBN 978-86-7236-089-9

BIOINFORMATICS EDUCATION IN SLOVENIA FROM AN IT PERSPECTIVE

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In this paper we intend to give insight into preparations of the 2nd Bologna cycle study programme of Bioinformatics at the University of Maribor in 2006, the start of the study programme in 2008 and the first follow-up after the 6 completed years of study in 2014.

This was one of the first 2nd Bologna cycle study programmes of Bioinformatics in this part of the Europe and as such, prepared a lot of challenges for the authors. Being an interdisciplinary study programme and requiring a wide variety of experts, was the first challenge. Coping with students coming from different backgrounds, was the second challenge. Modifying the study programme, managing requirements and changes in the environment, and growing together with the discipline was the third.

In Slovenia the study programme has been designed in accordance with legal requirements and is technically logical, consistent and modern in content. The fundamental objectives and learning outcomes of the programme are congruent with the content and level of the study programmes; general and course-specific competences have been defined separately for each study programme.

The study programme is internationally comparable. Comparison was carried out with more than three related foreign programmes from different countries, of which at least two were from EU Member States. Study requirements were evaluated according to the Criteria for the Allocation of Credits to Study Programmes under the ECTS, the percentage of elective components in the programme were defined and syllabuses were enclosed. Important part have been also criteria for transferring between programmes which are in accordance with higher education legislation and criteria for transferring between study programmes.

Since the majority of the core team that prepared the study programme came from the Faculty of Electrical Engineering and Computer Science, we will give an insight from the IT specialist perspective.

Keywords: bioinformatics, education, information technologies

 ISBN 978-86-7236-089-9

BIOPTRON HYPERPOLARIZED NANO-PHOTODYNAMIC LIGHT THERAPY IN MEDICINE

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BIOPTRON light therapy is a family of polarized light devices with specific properties, including a polychromatic range of wavelengths in the visible and near infrared light spectrum. The characteristics of BIOPTRON polarized light have been well documented. The most clinically useful wavelengths of BIOPTRON light include red light, due its anti-inflammatory properties, stimulation of skin fibroblasts to synthesize collagen and elastin proteins for wound healing and anti-aging uses, and for its stimulatory effect on microcirculation. BIOPTRON light also inhibits microbial infections (blue wavelengths) and has a positive effect on the immune system. Cancer treatments have evolved significantly through the years. The combination of light and photosensitizers for phototherapeutic interventions, such as photodynamic therapy, has transformed medicine and biology. Recent advances have combined the use of light sensitizing targeted treatments for more superficial tumours and cancers to produce cytotoxic reactive oxygen species. Metal nanoparticles can be injected into the bloodstream so that they accumulate in tumours. When the proper wavelength of light is shined on these nanoparticles from outside the body, plasmon oscillations generate heat, thereby damaging tumour cells. In essence, a photosensitive source of free radicals can be activated by light to destroy cancer. Laser-based treatments are limited to superficial or endoscope-accessible lesions. Research efforts are therefore being focused on strengthening the ability of light to penetrate the body. Polarized light is superior to diffuse light with respect to depth of tissue penetration because the vibrations occur in a single plane. We have developed hyperpolarized light, which results in 25-30% greater tissue penetration than polarized light. Our studies in animal models demonstrate that hyperpolarized light increases the tissue effects of nanoparticles. Nanoparticle design can be tailored for the specific frequencies of hyperpolarized light, in relation to the sensitizing or nanoparticle agent, the result being improved depth of tissue penetration combined with improved yield of tissue destruction by various cytotoxic mechanisms. In addition, these advances may impact on other non-destructive physiologic effects of light therapy on tissue healing and immunity, microcirculatory health, and anti-aging.

 ISBN 978-86-7236-089-9

MRI-CONTRASTED AU-FE_3O_4 HYBRID NANOPARTICLES FOR ADVANCED RADIOTHERAPY

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Radiosensitizers are used to improve the efficacy of radiotherapy inducing sensitization of cancer cells to radiations. Current radiosensitizers are limited because of the lack of techniques to monitor their biodistribution after administration, preventing reliable prognosis of treatment. Alternative methods can exploit properly designed nanoparticles which can be tracked via MRI and offer radiotherapy enhancement.

In this work, gold-magnetite hybrid nanoparticles (H-NPs) are proposed as a theranostic tool able to enhance the cell killing activity of radiations while being real-time monitored by magnetic resonance imaging (MRI). In H-NPs, gold would scatter megavoltage radiations and would release secondary electrons generating free radicals able to fix DNA radiation-induced damages and enhancing the effects of radiations in terms of reduction of the surviving fraction of irradiated cells as shown by *in vitro* and *in vivo* studies [1,2]. On the other hand, magnetite would permit the MRI tracking and quantification of the nanoparticles, allowing the tailoring of the radiation treatment thanks to the estimation of the amount of gold in the cancer tissue [3]. Hydrophilic, gold core and magnetite shell H-NPs of about 30 nm in diameter were prepared and their performance as MRI-probes and radiosensitizers were investigated *in vitro*. Size, chemical composition and stability in physiological conditions were evaluated by transmission electron microscopy, ion-coupled plasma optical emission spectroscopy and dynamic light scattering. The potentialities of H-NPs as contrast agent for MRI were estimated by nuclear magnetic resonance spectroscopy, revealing that H-NPs significantly affect the T2 relaxation time even at very low concentration. Confocal microscopy and cell membrane integrity assay, on human osteosarcoma MG63 and murine fibroblast 3T3 cell cultures exposed to H-NPs, demonstrated that nanoparticles were internalized by cells and did not induce cytotoxicity.

Keywords: hybrid nanoparticles, theranosis, radiotherapy, MRI tracking

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 ISBN 978-86-7236-089-9

NEW HOPE FOR ERADICATION OF HIV FROM THE BODY: THE ROLE OF POLYMERIC NANOMEDICINES IN HIV/AIDS PHARMACOTHERAPY

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Human immunodeficiency virus continued to be the greatest challenge and killer disease of the 21st century despite the advent of potent highly active antiretroviral therapy which are limited by their severe adverse effects, significant drug interactions, frequent dosing, limited bioavailability, and less access to viral reservoir sites like macrophages. Nano-medicines are becoming new hopes in avoiding these shortcomings of conventional antiretroviral drugs. The emphasis of this review is mainly the application of polymers based nanomedicines in pharmacotherapy of HIV/AIDS. Most of the studies to date on this area are *in vitro* and human clinical trials are totally missed. However, many interesting points are uncovered through this review like the possibility of achieving high intracellular concentration of drugs, very good antiretroviral activity, improved bioavailability, reduced toxicity and release of the drugs from nanocarriers for long time reducing the need for frequent dosing. Indeed, a lot of assignments left behind for researchers to overcome the challenges hindering the wider application of nanomedicines in treatment of HIV/AIDS.

Keywords:

HIV/AIDS; Antiretrovirals; Nano-polymers; Nanomedicines

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 ISBN 978-86-7236-089-9

CONTROLLED DRUG DELIVERY BY POLYMER-GOLD NANOCONJUGATES

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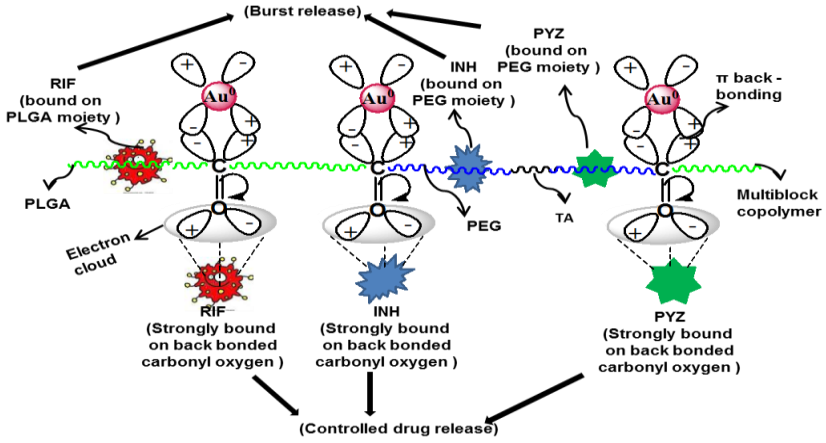
A series of new multiblock copolymers of poly (lactic-co-glycolic) acid (PLGA) – polyethylene glycol (PEG) – tartarate (TA) – polyethylene glycol (PEG) – poly (lactic-co-glycolic) acid (PLGA) has been synthesized by melt polycondensation technique. The conjugation of AuNPs via the formation of π-back-bonding with the carbonyl group of the multiblock copolyesyter has been investigated for tuberculosis multi drug delivery. The biocompatibility of multiblock copolymers and AuNPs nanoconjugates was investigated by the *in vitro* cytotoxicity study on vero cell line. The three major tuberculosis drugs viz. rifampicin, isoniazid and pyrazinamide loaded AuNPs conjugated multiblock copolymers were prepared by probe-sonication followed by self-assembly method. The in-vitro drug release experiment was carried out and the amount of the three drugs released at various time intervals was determined simultaneously by HPLC technique. The nanoconjugates exhibit 33 – 40 % of RIF, 71 – 95 % of INH, 77 – 99 % of PYZ loading efficiencies, while the polymer NPs exhibit relatively lesser values. The nanoconjugates show sustained drug release up to 264h.The formation of π-back bonding in the AuNPs-polyester nanoconjugates enhances high electron density on the carbonyl oxygen which results in better drug loading and sustained drug release behaviour.



Key words: multiblock copolymer; PLGA-PEG-TA-PEG-PLGA; Au Np ;Controlled delivery

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 ISBN 978-86-7236-089-9

COATING POLYURETHANE SURFACES BY ELECTROSTATIC CHARGING FOLLOWED BY DIP COATING/ELECTROPHORETIC DEPOSITION

Garima Bhardway

Aim: Surface associated infections are one of the main causes for failures associated with medical devices. Bacterial localization and biofilm formation may lead to acute and chronic infection. Biofilm on the surface protects the bacteria from the immune system and antibiotic therapy. This needs aggressive treatment of antibiotics. The high doses of antibiotic treatment prevent healthy tissue formation at the site and triggers antibiotic resistance. Thus, to prevent infections, various strategies have been developed besides conventional systemic and local antibiotic treatment. Recently, there is an increasing interest for coating these surfaces to improve bioactivity and prevent infection. The current study aimed to modify the surface of polyurethane endotracheal tubes by charging them electrostatically and then coating them with the anti-bacterial protein CSA-13 via dip coating and electrophoretic deposition.

Method: A positive charge was induced on the surfaces of the polyurethane endotracheal tubes by rubbing them with wool for 5 minutes each on the inside and the outside. Then these tubes were coated with the biological entity CSA-13, which is known to inhibit bacterial infection. The coating was achieved by 2 methods:

1.) **Dip coating:** The samples were dipped in the CSA-13 solution for a minute each 3 times.

2.) **Electrophoretic Deposition:** Titanium foil purchased from Alfa Aesar (Catalog number 10385) was used as both the counter and working electrode and the CSA-13 solution was used as the electrolyte. The polyurethane tube was placed around the negative electrode and this allowed the tube to get coated. A voltage of 20 V was used for a time period of 10 minutes.

These tubes were then allowed to dry at room temperature and then visualized using SEM to confirm coating.

Results and conclusion:

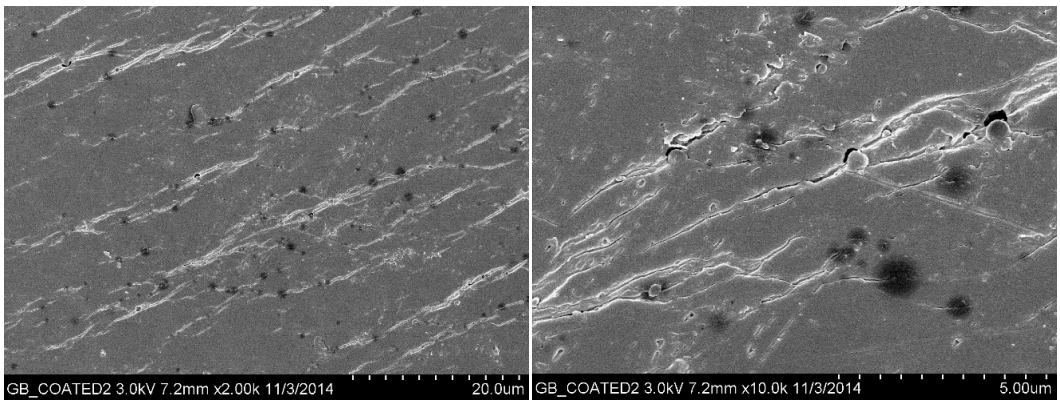

Figure 1: SEM images of the coated surfaces (a), (b)

A thick and uniform coating was achieved on both the inside and outside surfaces of the tubes. Bioactivity of the protein was maintained and the entire process was cost and time efficient.

Acknowledgements: The authors would like to thank N8 and Northeastern University for funding.

 ISBN 978-86-7236-089-9

ELECTROSPUN SILK DOPED WITH SELENIUM NANOPARTICLES TO ENHANCE ANTIBACTERIAL PROPERTIES

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Introduction: Skin infections cause 7-10% of all hospitalizations in the United States, with the vast majority caused by bacterial infections.[1] The best defense against infection is to maintain healthy skin tissue to ward off bacterial infection and other environmental factors. Silk is well characterized and has been demonstrated to possess beneficial properties for skin applications.[3] However, silk has poor antibacterial efficacy[4] whereas selenium nanoparticles demonstrate good antibacterial properties[5]. By incorporating the selenium nanoparticles into electrospun silk scaffolds, we hope to improve on an otherwise ideal skin biomaterial.

Materials and Methods: Silk was extracted from *Bombyx mori* by the Rockwood's protocol[6] while selenium nanoparticles were synthesized by Tran's protocol[7]. Extracted silk was resuspended in formic acid at 8-14%, w/v, and spun at flow rate of 0.75 mL/hr, distance to a collector at 10cm, and at a voltage at 20kV. *Staphylococcus aureus* (ATCC -10832D-5) was cultured on the substrates with 1, 0.1, 0.01, and 0.001 mg/mL selenium nanoparticles in 0.3% tryptic soy broth (Sigma-Aldrich). After 24 hrs, 20 µL of bacterial solution was plated to determine the colony forming units (CFU)/mL. Experiments were conducted in triplicate. The electrospun scaffold was characterized by SEM and goniometry to determine the physical make-up of the scaffolds, with and without selenium nanoparticles. Selenium nanoparticles were characterized by DLS to determine particle size and dispersity.

Results and Discussion: Electrospun scaffolds possessed fiber diameter of 1-200 nm and pore sizes of ~2µm. Surface contact angle was 30º, showing a hydrophilic surface. Results of this study showed 1 log inhibition of *S. aureus* in the presence of selenium nanoparticles (Figure 1).

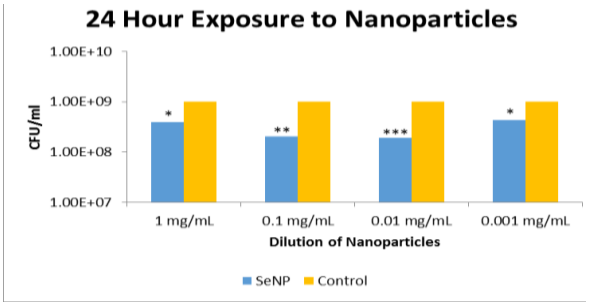

Figure 1. Bacterial density after contact with 1, 0.1, 0.01, and 0.001 mg/mL concentration of selenium nanoparticles. All selenium treated samples displayed significant difference from control. N=3. * = P<0.02 from control, ** = P<0.005, *** = P<0.004

Conclusions: Selenium nanoparticles inhibited *S. aureus* growth at all test concentrations. Electrospun silk generated fiber diameters ~200 nm and micron sized pore sizes, ideal for mammalian cellular adhesion.

ISBN 978-86-7236-089-9

Acknowledgements: The authors thank William Fowle, Scott McNamara, and the Northeastern University Department of Chemical Engineering for facilities and funding.

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 ISBN 978-86-7236-089-9

POTENTIAL OF CERIUM OXIDE NANOPARTICLES AS REACTIVE OXYGEN SCAVENGERS

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As one of the novel nanoparticle chemistries, nanoscaled cerium oxide has proven to be a promising candidate in numerous biological applications[1]. Some of nanoceria's potential applications in regenerative medicine include support for cell survival, modification of cell proliferation[2]. Recently it has been reported that nanoceria can scavenge reactive oxygen species, including superoxide radical, hydrogen peroxide and hydroxyl radicals due to its unique ability to switch its oxidation state from Ce^{+3} to Ce^{+4} [3]. Nanoceria were synthesized via alkaline based precipitation method. MTS assays were performed with human dermal fibroblast cells. Cells were seeded at a density 5,000 cells/well, allowed to adhere for 24 hours and the following day, in order to determine the cyto-protective function of ceria nanoparticles, cells were preincubated with ceria at a 50, 250, 500, 1000 μg/mL concentration for 2, 4, 8, and 16 hours. Following pre-incubation, cells were treated with different (1 mM, 1.5 mM, 1.75 mM) H_2O_2 concentrations for another 24 hours. After 24 hours of incubation, the MTS assay for cell viability and carboxy-H_2DCFDA assay to quantify ROS generation were performed. 0.1 M dextran coated, sub 5 nm nanoceria (DCN) were synthesized, and utilized to rescue HDF cells. Cells were rescued when they were pre-incubated with 0.1 M DCN before being exposed to non-specific ROS source H_2O_2 in a time and concentration dependent manner. Results suggested that as nanoparticle concentration, and pre-incubation time was increased, its capacity to scavenge higher molarity H_2O_2 was enhanced. ROS assay results also suggested that viability of the cells were directly correlated with the ROS amount that the cell produced. 0.1 M DCN particles caused a decrease in ROS generation in the presence of non-specific ROS. The results showed that ceria treated cells were able to recover from the oxidative damage /cytotoxicity exerted by the drugs which suggests that ceria nanoparticles may act as antioxidants within the body.

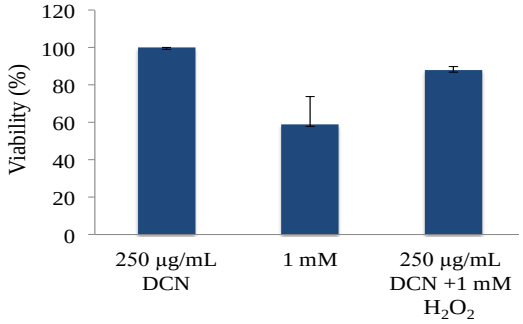

Figure 1. Viability results of HDF when they were pre-incubated with 250 μg/mL dextran coated cerium oxide nanoparticles cells for 2 hours before being exposed to H_2O_2 for 24 hours. Data=mean ±SEM

Keywords: Nanoceria, reactive oxygen species

 ISBN 978-86-7236-089-9

Acknowledgements: Dr. Hilal Yazici is supported by TÜBİTAK – BİDEB, International Postdoctoral Research Scholarship Programme (Programme Number: 2219). The authors also thank Northeastern University for funding.

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 ISBN 978-86-7236-089-9

SKIN PERMEABLE PEPTIDE AMPHIPHILES FOR COSMETIC APPLICATIONS

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One of the most predominant symptoms of skin aging is wrinkle formation, which resulted from both intrinsic aging and environmental damage, such as chronic exposure to UV radiation. Current anti-aging and anti-wrinkle materials often induce a toxic response, which results in inflammation, to increase tissue growth under the skin. Although effective, a much safer and more effective way to alleviate the effect of aging and thereby winkle formation need to be developed. Several biomimetic peptide sequences[1] (KTTKS, GQPR, GHK etc.) have been identified as structural mimics of type I collagen to be effective in stimulating synthesis of key constituents of extracellular matrix by fibroblasts, however, they typically suffer from poor skin penetration. Incorporation of cell penetrating peptides (CPPs) has been an emerging strategy to transport a variety of cargo across cellular membrane in a dose dependent manner.[1] In this study, peptide amphiphiles that consist of both CPPs and biomimetic sequences was designed and characterized. The abilities of these peptide amphiphiles to penetrate the skin, to scavenge free radicals, and to promote fibroblast functions (specifically, increasing adhesion, proliferation, collagen synthesis, and decreasing elastase and collagenase synthesis) were determined.

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 ISBN 978-86-7236-089-9

UNDERSTANDING THE ROLE OF NANOSCALE TOPOGRAPHY OF POLYMER SURFACES ON INHIBITING BACTERIAL ADHESION AND GROWTH FOR CATHETER APPLICATIONS

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Here, we present a simple and cheap method to prepare a nano-patterned polydimethylsiloxane (PDMS, a commonly used catheter material) replica by using highly ordered nanotubular anodized titanium as the template [1]. In vitro bacterial studies using *Staphylococcus aureus*, *Escherichia coli* were conducted to assess the effectiveness of the nano-patterned PDMS (nano-PDMS) at inhibiting bacterial growth [2]. In addition, human fibroblast and endothelial cell assays were conducted to determine the influence of the nanostructure on mammalian cell behaviour as a measurement of toxicity. To elucidate the mechanisms of how surface nano-topographies affect cell/ bacteria adhesion, protein interactions with different surfaces were also investigated by using the bicinchoninic acid (BCA) protein assay.

As expected, the nano-patterned structures were fabricated successfully on the surface of PDMS. Results showed that nano-PDMS inhibited the growth of both two bacteria after 24h and 48h, respectively. Moreover, data suggested the effectiveness of bacteria inhibition reached above 50%, all without employing antibiotics. It was also found that nano-PDMS increased both fibroblast and endothelial cell adhesion. BCA protein results indicated that the increase of nanoscale surface roughness caused a significant increase of the amount of adsorbed proteins, presumably due to the increased surface area and change of adsorption sites (Fig.1). The maximum adsorbed protein occurred at an incubation time of approximately 1h. The adsorbed mass subsequently decreased during the next couple of hours of incubation due to the Vroman effect. The increased protein adsorption on the nano-PDMS in the first several minutes could in part be responsible for the bactericidal properties.

The relationship between the nano-topography, protein adsorption and bacterial activities was investigated in this study. Data shows that the nano-topography on PDMS could increase the amount of protein adsorbed, inhibit both bacterial adhesion and growth significantly while remaining non-toxic to mammalian cells, and thus should strongly be considered for reducing catheter-associated infections.

ISBN 978-86-7236-089-9

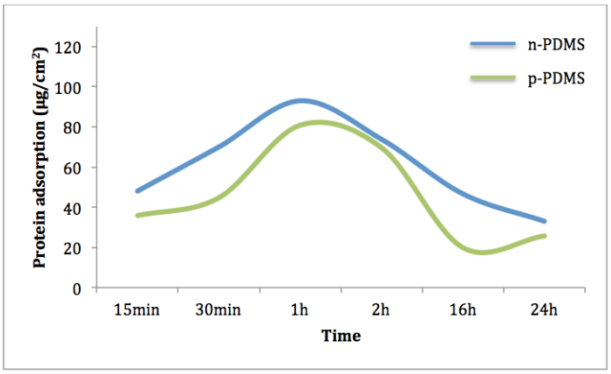

Figure 1. Variation of the amount of protein adsorbed on PDMS surfaces with (and without) nanostructure as a function of incubation time in tryptic soy broth (TSB) media. N = 3. Abbreviations: n-PDMS (nano-patterned PDMS); p-PDMS (plain-PDMS).

Key words: Nanofabrication, PDMS, infection, catheter

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 ISBN 978-86-7236-089-9

SELECTIVE INHIBITION OF OSTEOSARCOMA CELL FUNCTIONS INDUCED BY CURCUMIN-LOADED SELF-ASSEMBLED ARGININE-RICH-RGD NANOSPHERES

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Objectives: To develop a treatment against osteosarcoma with higher selectivity towards osteosarcoma cells and lower cytotoxicity towards normal osteoblast cells.

Statement of methods: Curcumin was found to have significant selectivity against osteosarcoma cells in vitro, and the ampiphilic peptide C18GR7RGDS was designed, fabricated and used as a curcumin carrier in aqueous solution. This peptide contains a hydrophobic aliphatic tail group leading to their self-assembly by hydrophobic interactions, as well as a hydrophilic head group having arginine-rich and an arginine-glycine-aspartic acid (RGD) structure, which may lead to efficient cell penetration and targeting for cancerous cells since RGD sequence can target to the overexpressed $\alpha v\beta 3$ integrin. Using a method of co-dissolution with acetic acid and dialysis tubing, the solubility of curcumin was enhanced and formed a homogeneous solution with the help of amphiphilic nanoparticles (APNPs). This study investigated the selectively inhibitory effect of the APNP/curcumin complexes against osteosarcoma cells. The cytotoxicity and cellular uptake of these materials on both osteosarcoma and normal healthy osteoblast cell lines were evaluated by 3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide (MTT) assays and confocal fluorescent microscopy.

Results: It was demonstrated for the first time that APNPs formed nanospheres with diameters of 10-20 nm in water and phosphate buffer saline (PBS), and opened up when the pH value was reduced to 4. Most importantly, the successful encapsulation of curcumin in APNPs was confirmed by Fourier transform infrared (FT-IR) and X-ray diffraction (XRD) analysis. The curcumin-loaded APNPs exhibited a significant selective cytotoxicity against the MG-63 osteosarcoma cell line compared to normal healthy osteoblasts.

Conclusions: APNPs can encapsulate hydrophobic curcumin in their hydrophobic cores, and the curcumin-loaded APNPs could be an innovative hydrophobic drug carrier for the selective inhibition against osteosarcoma cells than healthy osteoblasts.

Key words: Osteosarcoma, self-assembled, amphiphilic peptide, curcumin, selective inhibition

 ISBN 978-86-7236-089-9

DI-PEPTIDE-MODIFIED GEMINI SURFACTANTS AS GENE DELIVERY VECTORS: EXPLORING THE ROLE OF THE ALKYL TAIL IN THE PHYSICOCHEMICAL CHARACTERISATION AND THE BIOLOGICAL ACTIVITY

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Gene therapy holds a promising future for the treatment of many acquired and inherited diseases. However, one of the major hurdles for the successful application of gene therapy is still the effective delivery of genetic material into the targeted cells *in vitro* and *in vivo*. Di-cationic gemini surfactants are special category of drug carrier that showed promising results in delivering DNA. They have the ability to compact the negatively charged DNA through the electrostatic interaction forming nano-sized lipoplexes. Our aim is to elucidate the structure-activity relationship of di-peptide-modified gemini surfactant-based carriers.

Three glycyl-lysine modified gemini surfactants that varied in the length and degree of saturation of their alkyl tail were used to engineer DNA nanoparticles at nitrogen to phosphate charge ratios (N/P) of 1, 2.5, 5, 10, 15 and 20. To probe the optimal N/P ratio in the presence of helper lipid, in vitro gene expression and cell toxicity measurements were carried out. Characterization of the nanoparticles was accomplished by measuring the particle size and surface charge using dynamic light scattering and laser Doppler velocimetry, respectively. Morphological characteristics and the supramolecular assembly of the nanoparticles were studied using small angle X-ray scattering (SAXS) technique. Lipid packing parameter was studied using Langmuir-Blodgett trough.

The highest activity of glycyl-lysine modified gemini surfactants was observed with the 16-carbon tail compound at 2.5 N/P ratio showing a 5-10 fold increase in the level of reporter protein compared to the 12 and 18:1 carbon tail compounds. In addition, it exhibited the highest cell viability (85%) among the tested compounds. The nanoparticles had particle size of 81±6 nm, surface charge of +21±1 mV and adopted an inverted hexagonal phase which is conducive to cellular penetration. Moreover, the 16-carbon tail compound exhibited the larger mean molecular area of 90 A^2 and lowest critical micellar concentration of 0.155 mM.

We conclude that the structure of the gemini surfactants play an important role in determining the gene transfer efficiency of the delivery system.

Key words: Gene delivery, Di-peptide-modified gemini surfactants, Transfection efficiency, Small angle x-ray scattering

 ISBN 978-86-7236-089-9

SYNTHESIS, STRUCTURAL CHARACTERIZATION AND APPLICATION OF CADMIUM SULFIDE NANOCRYSTALS WITH FLUORESCENT DYES FOR SOLAR ENHANCEMENT

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Cadmium sulphide nanocrystals (CdS NCs) of ≈ 7.0 nm have been synthesized and structurally characterized with X-Ray diffraction (XRD), high resolution transmission electron microscope (HR-TEM) and topographical 3D image by atomic force microscopy (AFM). The binding and kinetic energies of 5th electron of 3d orbital (inner 3d5/2) and 3rd (outer 3d3/2) of Cd were 405.93 and 412.67 eV as well as 1074 and 1080.76 eV respectively determined with XPS. Thermogravimetric analysis (TGA) exhibited an initial transition from 550 to 800oC with 7.90 to 10.84 % weight losses by moderate thermal stability attributed to a strong binding energy. 100 μM CdS NPs with fluorescent dyes (FD) Rhodamine (RB), Sulphorhodamine (SRB) and Carboxyfluorescein (CF) were disperse in water, methanol and ethanol separately and studied.

Increased UV-Vis absorbance has been observed in the order (RB-CdS) > (SRB-CdS) > (CF-CdS). Probably the functional groups of the dyes has been the functionalized by CdS that could have induced the ◎-conjugated bonds to detain higher UV-Vis abs especially one -COOH plus four –CH2CH3, two -SO3 groups plus four –CH2CH3 and two -COOH plus one >C=O with one hydroxyl group respectively. Thus, the CdS-Dye-UV-Vis model proposed as new finding of our studies.

Keywords: CdS NCs; Crystal Structure; Photoelectrons; Fluorescent Dyes; SAED patterns

 ISBN 978-86-7236-089-9

DEVELOPMENT OF MAGNETIC NANOPARTICLES (MNPS) ENACPSULATED MILTEFOSINE NANOPARTICLE DRUG DELIVERY SYSTEM AGAINST *LEISHMANIA DONOVANI*

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Delivery of drug at target site are a promising technology to increase the maximum mechanism of action with minimum dose of requirement, Therefore we have developed the MNPs encapsulated Miltefosine nanoparticles drug delivery system to target macrophage of infected tissues against leishmaniasis for the optimum antileishmanial activity. The analyses of detailed structural characterization performed by transmission electron microscopy (TEM) confirmed the nano-size of the particle (size range of 10-20 nanometer and average size of nanoparticles dynamic light scattering (DLS)) for antileishmanial drug encapsulation confirmation. The dose of miltefosine is decreased by fifty percent as the IC50 value from 0.2 to 0.1 microgram thus two fold increase the efficacy of drug.Further inhibition of amastigotes in the splenic tissue with these nano carrier significantly more than with conventional miltefosine and Amphoterecin B.

Keywords: miltefosine, electron microscope, nanometer, Leishmaniasis

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 ISBN 978-86-7236-089-9

INTRINSIC ANTI-PROLIFERATIVE, ANTI-MIGRATORY AND PRO-APOPTOTIC FEATURES OF MULTIWALLED CARBON NANOTUBES IN CANCER CELLS

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Environmental selection forces and cellular adaptive strategies that lead to drug resistance also govern the cancer cell development. In this sense, the use of nanomaterials in medical sciences has the potential to completely transform the traditional anti-neoplastic treatments. Among nanomaterials, carbon nanotubes (CNT) represent a class of highly versatile materials, which display exceptionally interesting mechanical, thermal, electronic and biological properties. It has been demonstrated that MWCNTs can penetrate inside tissues and cells, where they disperse in the cytoplasm and intermingle with most cellular structures. These nanomaterials display interesting biomimetic properties that prompt their association with some of the intracellular nanofilaments such as DNA(1), actin(2) or microtubules(3), triggering anti-proliferative(3), anti-migratory(4) and cytotoxic effects(5) that can be exploited to defeat cancer.

Microtubules are fundamental cytoskeletal polymers ubiquitous in all eukaryotic cells, key players in many cellular processes such as cell division, migration and intracellular organization. These protein polymers have long been considered ideal targets of many anticancer therapies.(6) Indeed, microtubule binding drugs are among the most important chemotherapeutic agents available active against a broad range of cancers, including taxol ® or the vinca alkaloids. We have now confirmed the antineoplastic effect in vitro of MWCNTs of several human cancer cell lines included, HeLa (epitheloid cervix carcinoma), MCF7 (breast adenocarcinoma), SY-SH5Y (neuroblastoma), Ma-Mel-4 (melanoma), U87 (glioblastoma), etc in vitro. In all instances, MWCNT-treated cells display significant anti-proliferative, anti-migratory and pro-apoptotic effects compared to controls.

Understanding the relationship of particular nanomaterials with specific tissues, cells or proteins allows comprehending the molecular mechanisms underlying these biosynthetic interactions, opening new alternatives in nanomedicine. These properties of MWCNTs can be used in the battle against cancer to boost the effect of classical microtubule-binding chemotherapies, as neo-adjuvant or adjuvant therapies.

Keywords: tubulin, biomechanics, mitosis, cancer, chemotherapy

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 ISBN 978-86-7236-089-9

BIO-COMPATIBILIZATION OF MULTI-WALLED CARBON NANOTUBES BY IMPROVING IN VIVO DEGRADATION

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Carbon nanotubes (CNTs) are highly appealing in nano-bio-technology. These nanomaterials display interesting mechanical, thermal, electronic and biological properties, are capable to move across cellular barriers, including the blood-brain-barrier, can interact with tissues in living organisms and finally can translocate inside the cells. Multiwalled carbon nanotubes (MWCNTs) in particular, display intrinsic biomimetic properties that prompt their association to microtubules in vitro(1) and in vivo,(2) triggering interesting anti-proliferative, anti-migratory(3) and cytotoxic properties(4). Unfortunately, these interesting properties of CNTs due to their bio-mimetics with the naturally occurring intracellular filaments are a double edge-sword since CNTs can inherently trigger genomic instability, and thus, carcinogenesis. In this sense, bio-compatibilization of CNTs improving in vivo degradation or elimination is a "must" to produce viable nanomedicine against cancer. Yet, these nanomaterials are some of the most stable, strongest and stiffest materials known to man.(5)

Recent studies show that CNT can be degraded in different biological contexts.(6–8) In particular, macrophages,(9–11) key components of malignant tumors,(12) are some of the cells that have the capacity to destroy enzymatically CNTs. Here we demonstrate how different MWCNT pre-treatments to improve degradation in vivo, in cultured macrophage cells. These results provide strategic clues of how to improve MWCNT degradation and elimination to reduce their accumulation after tumor treatment in different tissues.

Keywords: biodegradation, carbon nanotubes, tumour, chemotherapy

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 ISBN 978-86-7236-089-9

ENCAPSULATION AND RELEASE OF RNA MOLECULES IN GELATIN-BASED NANOPARTICLES

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Gene therapy offers great opportunities for the treatment of severe diseases including cancer. In recent years the design of synthetic carriers for nucleic acid delivery has become a research field of increasing interest. Studies on the delivery of DNA have brought up a variety of gene delivery vehicles. The more recently emerged gene strategy by the intracellular delivery of RNA takes benefit from existing expertise in DNA transfer. Despite common properties however, delivery of RNA also faces distinct challenges due to apparent differences in size, stability of the formed nucleic acid complexes, the location and mechanism of action [1].

One of the challenges for the efficient intracellular delivery of therapeutic biomolecules after their cell internalization by endocytosis is to manipulate the non-productive trafficking from endosomes to lysosomes, where degradation may occur. The combination of the endosomal acidity with the endosomolytic capability of the nanocarrier can increase the intracellular delivery of many drugs, genes and proteins, which, therefore, might enhance their therapeutic efficacy [2]. Taking into account recent results in the preparation of gelatin-based nanoparticles containing DNA, this project aims the preparation and physicochemical characterization of new nucleic acid-based particles for the sustainable RNA delivery [3]. Gelatin (either high or low gel strength) and protamine sulfate has been selected to form particles by interaction of oppositely charged compounds. Particles in the absence of RNA (binary system) and in the presence of RNA (ternary system) have been prepared. The physicochemical characterization (particle size, polydispersity index, degree of RNA entrapment and DNA binding efficiency) have been evaluated as a function of the nature of the RNA derivative.

Keywords: RNA, nanoparticles, RNA entrapment, degree of complexation, stability.

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 ISBN 978-86-7236-089-9

GELATIN-BASED NANOPARTICLES FOR THE EFFICIENT INTRACELLULAR DNA DELIVERY

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The rapidly rising demand for therapeutic grade DNA molecules requires associated improvements in encapsulation and delivery technologies. One of the challenges for the efficient intracellular delivery of therapeutic biomolecules after their cell internalization by endocytosis is to manipulate the non-productive trafficking from endosomes to lysosomes, where degradation may occur. The combination of the endosomal acidity with the endosomolytic capability of the nanocarrier can increase the intracellular delivery of many drugs, genes and proteins, which, therefore, might enhance their therapeutic efficacy [1]. The gelification properties of gelatin as well as the strong dependence of gelatin ionization with pH makes this compound an interesting candidate to be used to the effective intracellular delivery of active bio macromolecules [2].

In the present work, gelatin (either high or low gel strength) and protamine sulfate has been selected to form particles by interaction of oppositely charged compounds. Particles in the absence of DNA (binary system) and in the presence of DNA (ternary system) have been prepared. The physicochemical characterization (particle size, polydispersity index and degree of DNA entrapment) have been evaluated. Cytotoxicity experiments have showed that the isolated systems and the resulting gelatin-based nanoparticles are essentially non-toxic. The pH-dependent hemolysis assay and the response of the nanoparticles co-incubated in buffers at defined pHs that mimic extracellular, early endosomal and late endo-lysosomal environments demonstrated that the nanoparticles tend to destabilize and DNA can be successfully released. It was found that, in addition to the imposed compositions, the gel strength of gelatin is a controlling parameter of the final properties of these nanoparticles. The results indicate that these gelatin-based nanoparticles have excellent properties as highly potent and non-toxic intracellular delivery systems, rendering them promising DNA vehicles to be used as non-viral gene delivery systems.

Keywords: DNA, nanoparticles, DNA entrapment, haemolysis, *in vitro* cytotoxicity.

References:

1) A. K. Varkouhi et al., *J. Control. Release,* 151 (2011) 220.
2) A. O. Elzoghby, *J. Control. Release*, 172 (2013) 1075.

 ISBN 978-86-7236-089-9

M.C. Morán acknowledges the support of the MICINN (Ramon y Cajal contract RyC 2009-04683). This study was financially supported by Project MAT2012-38047-C02-01 from the Spanish Ministry of Science and Innovation and FEDER, European Union. M.A. Busquets is grateful to the Spanish Ministry of Science and Innovation for financial support of the Project MAT2012-36270-C04-03. This work was conducted under the umbrella of COST CM1101 and MP1106 Actions.

 ISBN 978-86-7236-089-9

SUPERHYDROPHOBIC COATINGS FOR ANTIFOULING IN SHALLOW EUPHOTIC SEAWATER

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Highly water repellent coatings that expose contact angle above 150° and have a very small hysteresis, are known as superhydrophobic (SH) surfaces. The small area available for these surfaces, when in contact with water, are used in many applications where interactions with aqueous environment cannot be avoided such as materials protection and friction reduction in marine surrounding.

In this study development of the surface coatings applied for the protection of metal surfaces from fouling has been performed also with the aim to provide more resistant long lasting coatings. The SH surfaces here presented were prepared using different methodologies, and studied in presence of pure water, marine waters, solutions and dispersions.

Moreover, the project will try to incorporate capsule-like structures into the SH surfaces in order to obtain self-healing materials. In this preliminary stage, capsules have been prepared as a model for development of self-healing materials.

The on-field studies and surface characterization of SH surface have been carried out in order to test its behaviour in terms of fouling prevention and protection of metals in underwater conditions.

Acknowledgements:

The Authors acknowledge the RITMARE (La Ricerca Italiana per il Mare) Flagship Project and COST Action MP1106

 ISBN 978-86-7236-089-9

CYTOTOXICITY AND WETTABILITY STUDIES OF NOVEL LASER INDUCED MEDICINES IN BIOMEDICAL FABRICS

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Phenothiazines and their derivatives are known as non-antibiotics and possess some antimicrobial, fungistatic and fungicidal activities. They can inhibit the replication of bacteria, reaching DNA and intercalating between its bases. These drugs are photosensitive compounds; when exposed to white light or to UV radiation, they suffer modifications at molecular level, consisting in degradation of the parental compound and yield new photoproducts that may have specific bactericide effects. For speeding up this process a high energy laser beam was used to which phenothiazine solutions were exposed, in order to increase antibacterial activity of the resulting mixture. More of the research is needed to obtain data about the use of photosensitive drugs with antibacterial and possibly anticancerous properties, aiming to identify new ways to deliver them to target tissues.

In this sense, the safety evaluation of new products or ingredients destined for human use is crucial prior to exposure. It is worth noting that, because of the expense of animal testing in toxicology and pressure from both the general public and government to develop alternatives to *in vivo* testing, *in vitro* cell-based models may be more attractive for preliminary testing of new materials. The prediction of toxicity is difficult, but cytotoxicity screening, which is routinely used in drug screening, gives a good indication of potential adverse effects in cells. In addition, an important feature in the development of delivery systems for parenteral administration is to determine their ability to cause haemolysis by interaction with the cell membrane. Their direct use in solutions or on tissues or impregnation with them of materials applied in treatments of biological surfaces is of great interest. The knowledge about these materials surface properties is important when solutions of modified medicines are poured on them and they are further applied on treated surfaces, since these properties may control the delivery process of medicines to target tissues. The results reported in this work concern the study made on the stability of phenothiazine solutions in order to know the time limits within which exposed solutions are stable and may be used for applications. The study of the cytotoxic properties of the unirradiated and irradiated solutions is presented and their interaction with fabrics is evaluated in view of further biomedical applications.

 ISBN 978-86-7236-089-9

Keywords: laser, phenothiazine, haemolysis, *in vitro* cytotoxicity, fabrics.

M.C. Morán acknowledges the support of the MICINN (Ramon y Cajal contract RyC 2009-04683). This study was financially supported by Project MAT2012-38047-C02-01 from the Spanish Ministry of Science and Innovation. The authors from NILPRP acknowledge the financial support of CNCS – UEFISCDI project number PN-II-ID-PCE-2011-3-0922 and by the NUCLEU program project PN 0939/2009. A. Smarandache was supported by the project POSDRU/159/1.5/S/137750. This work was conducted under the umbrella of COST MP1106 Action.

 ISBN 978-86-7236-089-9

PREPARATION AND CHARACTERIZATION OF NANO-CALCIUM FROM CHICKEN EGGSHELL POWDERS FOR DENTAL HEALTHCARE APPLICATION WITH HEAT TREATMENT AND BALLMILLING METHODS

Novra A.Sandi[1]*, Alfin Darari[2], Harini Sosiati[3], Firas Khoirunnisa[4], Mulya Fitranda A.R[1], Alfiani Kurnia[4], Navilatul Ula[4], Indra Bramanti[4]

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There are several million tons of eggshells are being generated daily as bio-waste across the world. The wide availability and natural-biological origin of the eggshells, containing several trace elements such as calcium that essential and important for human and animal metabolism and cells regulation. In this study, we propose a cost-effective and straight-forward technique for converting calcium carbonate obtained from eggshells into nano-scale calcium via subsequent heat treatment and high energy ball-milling. The raw eggshell powders were calcinated for 6 hours at 900 °C were resulted to CaCO3, and for 12 hours were resulted to nano-scale (most predominantly 500 nm) CaO (calcium oxide). The samples then were treated by using high energy ball-milling with comparison respectively, 15:1 and 20:1 between weight of the balls and material within 30 minutes until 180 minutes. The characterization raw eggshell powder were analysed with x-ray diffraction (XRD) which is showed the peak of graphic at 2 theta (degrees) for CaCO3 (calcium carbonate) after 6 hours of calcination, and the CaO were observed after 12 hours of calcination. The photograph of nano-scale from CaO were observed using scanning electron microscope (SEM) with the scale most predominantly between 200-300 nm.

Keywords: Chicken eggshell powders, nano-calcium, heat treatment, ball-milling, dental application.

 ISBN 978-86-7236-089-9

PROGRAMME

ISBN 978-86-7236-089-9

SUNDAY JUNE 21

15:00-21:00 PM Registration/Conference Check-in

MONDAY JUNE 22

09:30-12:30 PM **SESSION I**
Chairmen: Thomas J. Webster and Djuro Koruga

09:30-10:00 AM Welcoming Remarks

10:00-10:45 AM *Plenary Talk*: **15 Years of Conducting Nanomedicine Research: Where are We Headed?**
Thomas J. Webster, Northeastern University, USA

10:45-11:15 AM *Invited talk:* **PH Dependent Antibacterial Activity of Dextran-coated Nanoceria**
Hilal Yazici, Ece Alpaslan, Thomas J. Webster, Northeastern University, USA, King Abdulaziz University, Saudi Arabia*

11:15-11:30 AM Coffee

11:30-11:50 AM **Stem Cells from Fat Tissue and Their Application - Pilot Study in Patients with Anal Fissures**
Katarina Andjelkov, Sforza M., Petrovic J., Krivokapic Z., BelPrime Clinic, University of Medicine, Belgrade, Serbia*

11:50-12:10 PM **Development of Pegylated PLGA Nanoparticle for Controlled and Sustained Drug Delivery in Chronic Myeloid Leukemia**
Sampath Malathi, Sengottuvelan Balasubramanian, Guindy Campus University of Madras, India*

12:10-12:30 PM **Raman & Fluorescence-based Multiplexed Realtime Imaging**
Dae Hong Jeong, Sinyoung Jeong, Yoon-Sik Lee, Keon Wook Kang, and Dong Soo Lee, Seoul National University, Seoul National University College of Medicine, Korea*

12:30-12:50 PM **Sers Nano Probes for Bio Applications**
Yoon-Sik Lee, Professor, School of Chemical and Biological Engineering, Pioneer Research Program Chair, Seoul National University, Korea

13:00-14:30 PM Break for Lunch

14:30-16:30 PM **SESSION II**
Chairmen: Alexander N. Kharlamov and Ljiljana Korugic-Karasz

ISBN 978-86-7236-089-9

15:00-15:30 PM *Invited talk*: **The Polymeric Thermoelectric Energy Harvesting Systems for Biomedical Applications Iodine-doped MEH-PPV Blends with Carbon Nanotubes**
Ljiljana Korugic-Karasz, Murat Tonga, Patrick S. Taylor, Eugene Wilusz, Frank E. Karasz, Paul M Lahti, University of Massachusetts, Natick Soldier RDE Center, USA*

15:30-15:50 PM **Investigation of the Hev Blue Light Blocking Effect of Nanophotonic Material**
Bozica Bojovic, Marija Tomic, Marina Nikolic, Dragomir Stamenkovic, Djuro Koruga, University of Belgrade, Zelezara Smederevo d.o.o., Optix d.o.o, University of Belgrade and European Centre of Peace and Development, Serbia*

15:50-16:10 PM **Characterisation of Photonic Nanomaterials for Contact Lenses, Before and After Exposure to External Magnetic Field by Spinner Magnetometer and Optomagnetic Imaging Spectroscopy**
Marija Tomic, Bozica Bojovic, Dragomir Stamenkovic, Lidija Matija, Djuro Koruga, University of Belgrade, Optix*

16:10-16:30 PM **Long-term Outcomes in Population Undergoing Plasmonic Photothermal Therapy of Atherosclerosis with Silica-gold Nanoparticles: Safety in Nanom-fim Trial**
Alexander N. Kharlamov, Ural Institute of Cardiology, Russia

17:00-19:00 PM **POSTER SESSION (1-10)**

TUESDAY JUNE 23

09:00-12:00 PM **SESSION III**
Chairmen: Alexander Majouga and Suzana Miljkovic

09:00-09:45 AM *Plenary talk*: **Water Based Nanomedicine: Diamagnetic / Paramagnetic Properties of Water, Healthy and Unhealthy Biological Tissues**
Djuro Koruga, University of Belgrade and European Centre of Peace and Development, Serbia

09:45-10:15 AM *Invited talk:* **Nanohybrid Magnetic Materials for Biomedical Application**
Alexander Majouga, Efremova M.V., Beloglazkima E.K., Rudakovskaya P.G., Zyk N.V., Golovin U.I.m Klyachko N.L., Panova E.I., Shetinin I.V., Sviridenkova N.V., Savchenko A.G., Lomonosov Moscow State University, Derzhavin Tambov State University, National University of Science and Technology, Russia*

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10:15-10:35 AM	**Remanent Magnetism on Nano and Pico Tesla Level of Biological Tissues** *Aleksandra Dragicevic*, Lidija Matija, Zoran Krivokapic, Andrej Ilankovic, Djuro Koruga, University of Belgrade, Clinical Centre of Serbia, University of Belgrade and European Centre of Peace and Development, Serbia*
10:35-10:50 AM	Coffee
10:50-11:10 AM	**Water Structured by Very Low Concentration of Fullerol: Implications for Dominant Role of Water in Their Antioxidant and Radioprotective Effects** *Jelena Muncan*, Ivana Mileusnic, Boris Kosic, Lidija Matija, University of Belgrade, Serbia*
11:10-11:30 AM	**Development of Moisturising Skin Care Product with Nano Harmonized Supstance** *Suzana Miljkovic*, Lidija Matija, Jelena Muncan, Jadran Bandic, Djuro Koruga, European University Novi Sad, University of Belgrade, ORS Hospital, University of Belgrade and European Centre of Peace and Development, Serbia*
11:30-11:50 AM	**Biophysics of Pain Suppression by Polarized Light and Near Infrared Irradiation: Exposure of Acupuncture Points on Nano Scale** *Sergiy A. Gulyar*, Zynaida A. Tamarova, Bogomoletz Institute of Physiology National Academy of Sciences of Ukraine, International Medical Innovation Centre Zepter, Ukraine*
12:00-14:00 PM	**POSTER SESSION (11-20)**
14:00-15:00 PM	Break for lunch
15:00-17:30 PM	**SESSION IV** *Chairmen: Alexander Majouga and Suzana Miljkovic*
15:00-15:30 PM	*Invited talk:* **Rapid Bone Regeneration with Nano-Hydroxyapatite Coated with a Chitosan-poly (d,l)-lactide-co-glycolide Bone-filling Material with Osteocondactive and Antimicrobial Properties** *Nenad Ignjatovic*, Uskokovic V., Ajdukovic Z., Mihajilov-Krstev T., Uskokovic D., Institute of Technical Sciences of the Serbian Academy of Science and Arts, Belgrade, Serbia, University of Illinois at Chicago, USA, University of Nis, Serbia*
15:30-15:50 PM	**MGO Nanomaterials Improve Cell Functions and Reduce Bacterial Infections for Orthopedic Tissue Engineering Applications** *Daniel J. Hickey*, Thomas J. Webster, Northeastern University, USA, Abdulaziz University, Saudi Arabia*

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15:50-16:10 PM **Silver Nanoparticle-embedded Polymersome Nanocarriers for the Treatment of Antibiotic-resistant Infections**
Benjamin M. Geilich, Anne L. van de Ven, Srinivas Sridhar, Thomas J. Webster, Northeastern University, USA, King Abdulaziz University, Saudi Arabia*

16:10-16:25 PM Coffee

16:25-16:45 PM **Selenium Nanoparticle Coatings for Anti-cancer, Anti-bacterial Bone Endoprostheses**
Michelle Stolzoff, Thomas J. Webster, Northeastern University, USA*

16:45-17:05 PM **Drug Releasing Implants Based on Nanoengineered Titania Nanotubes for Localized Bone and Cancer Therapy**
Dusan Losic, Karan Gulatu, Gagandeep Kaur, Shaheer Maher, Shafiur Rahman, Gerald J. Atkins, David M. Findlay, Andreas Evdokiou, University of Adelaide, Australia*

17:05-17.25 PM **Ultrastable Surfactant Free Metal Nanoparticles Study for Biomedical Applications**
Rauwel E., Rauwel P., Guha M., Lorena S. Gracia, Kuunal S., Wragg D., Tallinn University of Technology, Estonia, University of Oslo, Norway, University of Tartu, Estonia*

WEDNESDAY JUNE 24

09:00-12:00 PM **SESSION V**
Chairmen: Petra Povalej Bržan and Sergiy A. Gulyar

09:00-09:45 AM *Plenary talk:* **The Science of Entrepreneurship in Nanomedicine**
Aamir Butt, Nanomedical Accelerace, UK

09:45-10:15 PM *Invited talk:* **Aquaphotomic Study of Hydrated Hydroxylated Fullerene Based on Skin Nanocream: Water Based Nanomedicine**
Lidija Matija, Muncan J., Tsenkova R., Mileusnic I., Koruga D., University of Belgrade, Serbia, Kobe University, Japan, University of Belgrade and European Centre of Peace and Development, Serbia*

10:15-10:35 PM **Nanophysical approuch of endocervical and exocervical smears characterization using optomagnetic imaging spectroscopy**
B. Jeftic, M. Papic-Obradovic, L. Matija, Dj. Koruga, University of Belgrade, Europian Centre of Peace and Development, Serbia*

ISBN 978-86-7236-089-9

10:35-10:55 AM	**Bionformatics Education in Slovenia from an IT Perspective** *Milan Zorman, Peter Kokol, Gregor Stiglic, Petra Povalej Brzan*, Matjaz Debevc, University of Maribor, Slovenia*
10:55-11:15 PM	**BIOPTRON Hyperpolarized Nano-Photodynamic Light Therapy in Medicine** *Michael McNamara*, Sanja Vranic, Djuro Koruga, BIOPTRON AG, Wollerau, Switzerland and International Department of Biomedical Engineering and Nanomedicine, ECPD /University of Belgrade, Belgrade, Serbia*
11:15-11:45 PM	Coffee
12:00-13:00 PM	Workshop: **ECPD programs in nanomedical engineering and nanaomedicine** *Djuro Koruga, University of Belgrade and European Centre for Peace and Development, Serbia*
13:00 -15:00 PM	Break for lunch
15:00-17:00 PM	Workshop: **Start-up Companies in Nanomedicine** *Aamir Butt, Nanomedical Accelerace, UK*

THURSDAY
JUNE 25

09:00-10:00 AM	Books promotion: **Basic Knowledge, Clinical Symptoms and Treatment of Depression** *Authors: Sushil Sharma, Saint James School of Medicine, Bonaire, Dutch Caribbean, Netherlands* and **Introduction to Biomedical Chronodynamics** *Authors: Suzana Miljkovic, Bozica Bojovic, Djuro Koruga, DonVas, Belgrade, Serbia.*
10:00-10:15 AM	Coffee
10:30-20:00 PM	**Visit of Dubrovnik** or/and **Budva**

ISBN 978-86-7236-089-9

FRIDAY JUNE 26

10:00-11:00 AM **Award Ceremony, Closing Speeches**
Thomas J. Webster, Aamir Butt, Djuro Koruga

12:00 PM Departure Hotel

POSTER SESSION I (1-10)

P01. **MRI-contrasted Au-Fe_3O_4 Hybrid Nanoparticles for Advanced Radiotherapy**
Filippo Benetti, Devid Maniglio, Luca Minati, Aldo Valentini, Giorgio Speranza, Claudio Migliaresi, University of Trento, Fondazione Bruno Kessler, Azienda Provinciale pre I Servizi Sanitari, Italy

P02. **New Hope for Eradication of HIV from the Body: the Role of Polymeric Nanomedicines in HIV/AIDS Pharmacotherapy**
Jimma Likisa Lenjisa, Minyahil Alebachew Woldu, Gizaw Dabessa Satessa, College of Medicine and Health Sciences, Ethiopia

P03. **Controlled Drug Delivery by Polymer-Gold Nanoconjugates**
Mani Gajendiran, Sengottuvelan Balasubramanian, Guindy Campus University of Madras, India

P04. **Coating Polyurethane Surfaces by Electrostatic Charging Followed by dip Coating/Electrophoretic Deposition**
Garima Bhardwaj, Northeastern University, USA

P05. **Electrospun Silk Doped with Seleium nanoparticles to Enhance Antibacterial Properties**
Stanley Chung, Michelle Stolzoff, Batur Ercan, Thomas J. Webster, Northeastern University, USA

P06. **Potential of Cerium Oxide Nanoparticles as Reactive Oxygen Scavengers**
Ece Alpaslan, Hilal Yazici, Merlyn Vargas, Amit K. Roy, Jaime Gallego, Thomas J. Webster, Northeastern University, USA, Universidad de Antioqia UdeA, Colombia, King Abdulaziz University, Saudi Arabia

P07. **Skin Permeable Peptide Amphiphies for Cosmetic Applications**
Gujie Mi, Thomas J. Webster, Northeastern University, USA, King Abdulaziz University, Saudi Arabia

ISBN 978-86-7236-089-9

P08. **Understanding the Role of Nanoscale Topography of Polymer surfaces on Inhibiting Bacterial Adhesion and Growth for Catheter Aplications**
Luting Liu, Thomas J. Webster, Northeastern University, USA

P09. **Selective Inhibition of Osteosarcoma Cell Function Induced by Curcumin-Loaded Self-assembled Arginine-Rich-RGD Nanospheres**
Run Chang, Linlin Sun, Thomas J. Webster, Northeastern Univesrity, USA, King Abdulaziz University, Saudi Arabia

P10. **DI-Peptide-Modified Gemini Surfactants as gene Delivery Vectors: Exploring the Role of the Alkyl Tail in the Physicochemical Characterisation and the Biological Activity**
Mays Al-Dulaymi, Jackson Chitanda, Ronald Verrall, Pawel Grochulski, Ildiko Badea, University of Saskatoon, University if Saskatchewan, Canadian Light Source, Canada

POSTER SESSION II (11-20)

P11. **Synthesis, Structural Characterisation and Application of Cadmium Sulfide Nanocrystals with Fluorescent Dyes for Solar Enhancement**
Yashvant Raoa, Gajendra Inwatia, Man Singha, Central University of Gujarat, India

P12. **Development of Magnetic Nanoparticles (MNPs) Encapsulated Miltefosine Nanoparticle Drug Delivery System against *Leishmania donovani***
Rishikesh Kumar, Ganesh C Sahoo, VNR Das, Krishna Pandey, Sunil Kumar, Kalyani Trivedi, Yousuf Ansari, Sindhu Purva Rana, Manas Dixit, Rani Mansuri, Pradeep Das, Nanomedicine and Drug Discovery Department Agamkuan RMRIMS, India

P13. **Intrinsic Anti-Proliferative, Anti-Migratory and Pro-Apoptotic Features of Multiwalled Carbon Nanotubes in Cancer Cells**
Lorena Garcia-Hevia, Juan Villegas, Fidel Fernandez, Jesus Gonzales, Rafael Valiente, Monica L. Fanarraga, Universidad de Cantabria, Spain

P14. **Bio-Compatibilization of Multi-Walled Carbon Nanotubes by improving *in vivo* Degradation**
Jeroen Heuts, Hector Teran, Carmen Pesquera, Lorena Garcia-Hevia, Jesus Gonzales, Rafael Valiente, Monica L. Fanarraga, Universidad de Cantabria, Spain

P15. **Encapsulation and Release of RNA Molecules in Gelatin-based Nanoparticles**
Maria Carmen Moran, Ines Fornies, Guliem Ruano, M. Antonia Basquets, M. Pilar Vinardell, Universitat de Barcelona, Spain

ISBN 978-86-7236-089-9

P16. **Gelatin-based Nanoparticles for the Efficient Intracellular DNA Delivery**

Maria Carmen Moran, Neus Rosell, Guillem Ruano, M. Antonia Basquets, M. Pilar Vinardell, Universitat de Barcelona, Spain

P17. **Superhydrophobic Coatings for Antifouling in Shallow Euphotic Seawater**

Michele Ferrari, F. Cirisano, L. Liggieri, F. Ravera, E. Santini, A. Benedetti, CNR- Istituto per l' Energetica e le Interfasi, Italy

P18. **Cytotoxicity and Wettability Studies of Novel Laser Induced Medicines in Biomedical Fabrics**

Michele Ferrari, Tatiana Tozar, Agota Simon, Andra Dinache, Adriana Smarandache, Ionut Relu Andrei, Mihai Boni, Mihail Lucian Pascu, Francesca Cirisano and M. Carmen Morán, CNR- Istituto per l' Energetica e le Interfasi, Italy, National Institute for Laser, Plasma and Radiation Physics, Romania, Universitat de Barcelona, Spain

P19. **Preparation and Characterization of Nano-Calcium from Chicken Eggshell Powders for Dental Healthcare Application with Heat Treatment and Ballmilling Methods**

Novra A.Sandi, Alfin Darari, Harini Sosiati, Firas Khoirunnisa, Mulya Fitranda A.R, Alfiani Kurnia, Navilatul Ula, Indra Bramanti, Universitas Gadjah Mada, Diponegoro University, Indonesia

ISBN 978-86-7236-089-9