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WORK EXPERIENCE

Professor, Head of NanoBioPhysics Departement MedFUTURE Research Center for Advanced Medicine

"Iuliu Hatieganu" University of Medicine & Pharmacy [01/10/2018 – Current]

Address: Cluj Napoca (Romania)

City: Cluj-Napoca

Country: Romania

Teaching activities with the students/Ph.D. students from the Faculties of Pharmacy, General Medicine and Dentistry (romanian, french and english sections).
Research activities in the field of NanoBioTehnologies for medical applications
Coordinator of research activities in the field of Nanomedicine @ MedFUTURE - NanoBioPhysics Department

Associate Professor

"Iuliu Hatieganu" University of Medicine & Pharmacy [01/10/2013 – 30/09/2018]

Address: Cluj-Napoca (Romania)

Teaching activities with the students from the Faculties of Pharmacy, General Medicine and Dentistry (romanian, french and english sections).
Research activities in the field of NanoBioTehnologies for medical applications

Lecturer

"Iuliu Haţieganu" University of Medicine and Pharmacy [01/10/2011 – 30/09/2013]

Address: Cluj-Napoca (Romania)

Teaching activities with the students from the Faculties of Pharmacy, General Medicine and Dentistry (Romanian, French and English sections).
Research activities in the field of NanoBioTehnologies for medical applications

Assistent Professor

"Iuliu Haţieganu" University of Medicine & Pharmacy [01/10/2008 – 01/10/2011]

Address: Cluj-Napoca (Romania)

Teaching activities with the students from the Faculties of Pharmacy, General Medicine and Dentistry (romanian, french and english sections).
Research activities in the field of NanoBioTehnologies for medical applications

Scientific Researcher

'"Babeș-Bolyai" University [01/10/2007 – 01/10/2008]

Address: Cluj-Napoca (Romania)

Research activities in the field of NanoBioTehnologies using Near Field Microscopy/Spectroscopy & Ultrasensitive Vibrational Spectroscopy

PostDoctoral Researcher
Institute d'Electronique, Microelectronique et Nanotehnologie [01/09/2005 – 01/03/2007]

Address: Lille (France)

Research activities in the field of NanoBio Materials
Research activities in the field of inelastic electronic transport

Ph.D. Student
"Babes-Bolyai" University, Faculty of Physics [15/01/2004 – 01/05/2005]

Address: Cluj-Napoca (Romania)

Research activities in the field of nanostructured perovskites

Ph.D. Student
Universite Paris-Sud, XI [15/01/2003 – 14/01/2004]

Address: Orsay (France)

Research activities in the field on nanostrucured ceramics and High Temperature Superconductors (HTSC)

Ph.D. Student
"Babeș-Bolyai" University, Faculty of Physics [01/10/2002 – 14/01/2003]

Address: Cluj-Napoca (Romania)

Research activities in the field on nanostrucured ceramics and High Temperature Superconductors (HTSC)

EDUCATION AND TRAINING

Habilitation Thesis in Pharmaceutical Sciences @ UMF Cluj-Napoca
[23/09/2017]

Master in Pharmaceutical Sciences (Drug Analysis)
"Iuliu Haţieganu" University of Medicine and Pharmacy [01/10/2009 – 30/06/2010]

Address: Cluj-Napoca (Romania)

Pharmaceutical sciences & Drug analysis

Ph.D. in Physics
"Babes-Bolyai" University, Faculty of Physics [01/10/2002 – 25/05/2005]

Address: Cluj-Napoca (Romania)
Field(s) of study: Physics
Final grade: Cum Laudae
Thesis: Electrical and pinning properties of Bi:2212 superconductors doped by transition metals ions and containing artificial nanodefects

Solid state physics

Master in Physics
"Babeș-Bolyai" University, Faculty of Physics [01/10/2001 – 30/06/2002]

Address: Cluj-Napoca (Romania)

Licence in Physics
"Babeș-Bolyai" University, Faculty of Physics [01/10/1998 – 30/06/2001]

Address: Cluj-Napoca (Romania)

LANGUAGE SKILLS

Mother tongue(s): **Romanian**

Other language(s):

English

LISTENING C1 READING C1 WRITING C1

SPOKEN PRODUCTION C1 SPOKEN INTERACTION C1

French

LISTENING C1 READING C1 WRITING C1

SPOKEN PRODUCTION C1 SPOKEN INTERACTION C1

Italian

LISTENING A2 READING A2 WRITING A2

SPOKEN PRODUCTION A2 SPOKEN INTERACTION A2

PUBLICATIONS

Principal author or co-author of 75 scientific papers published in ISI journals in the field of physics, biophysics and nanomedicine.

According to WoS, for the whole scientific research activity, the H-index is 19, the number of publications 76, and more than 1000 citations. The total IF is ~ 320 ISI points.

In the last 10 years, more than 50 scientific papers were published in high-impact journals (Science, Pharmaceutics, Cancers, International Journal of Nanomedicine, Cell Death and Disease - Nature group, Scientific Reports, Physical Chemistry Chemical Physics, etc), achieving a total IF of over 210 points, an H-index of 17, and more than 600 citations.

According to Google Scholar the total H-index is 22 and the number of citations is ~1450.

https://scholar.google.ro/citations?hl=ro&tzom=-120&user=Msxs4qYAAAAJ

Nanoscale Investigation of DNA Demethylation in Leukemia Cells by Means of Ultrasensitive Vibrational Spectroscopy (Sensors, IF 3.847)

[2022]

A. Onaciu, V. Toma, C. Moldovan, A. B. Țigu, D. Cenariu,..., and R. Știufiuc*

DNA methylation is a crucial epigenetic hallmark of cancer development but the experimental methods able to prove nanoscale modifications are very scarce. Over time, Raman and its counterpart, surface-enhanced Raman scattering (SERS), became one of the most promising techniques capable to investigate nanoscale modifications of DNA bases. In our study, we employed Raman/SERS to highlight the differences between normal and leukemia DNA samples and to evaluate the effects of a 5-azacytidine treatment on leukemia cells. To obtain spectral information related to DNA base modifications, a DNA incubation step of 4 min at 94 °C, similar to the one performed in the case of RT-PCR experiments, was conducted prior to any measurements. In this way, reproducible Raman/SERS spectra were collected for all genomic DNA samples. Our Raman results allowed discrimination between normal and cancer DNAs based on their different aggregation behavior induced by the distinct methylation landscape present in the DNA samples. On the other hand, the SERS spectra collected on the same DNA samples show a very intense vibrational band located at 1008 cm−1 assigned to a rocking vibration of 5-methyl-cytosine. The intensity of this band strongly decreases in cancer DNA due to the modification of the methylation landscape occurring in cancers. We believe that under controlled experimental conditions, this vibrational band could be used as a powerful marker for demonstrating epigenetic reprogramming in cancer by means of SERS.

Co-delivery of gemcitabine and salinomycin in PEGylated liposomes for enhanced anticancer efficacy against colorectal cancer (The Journal of Liposome Research, IF 2.455)

[2022]

L. R. Tefas, I. Toma, A. Sesărman, M. Banciu, A. Jurj,..., and R. Știufiuc*

Colorectal cancer remains one of the major causes of morbidity and mortality in both developed and emerging countries. Cancer stem cells (CSCs) are a subpopulation of cells within the tumor mass harboring stem cell characteristics, considered responsible for tumor initiation, growth, relapse, and treatment failure. Lately, it has become clear that both CSCs and non-CSCs have to be eliminated for the successful eradication of cancer. Drug delivery systems have been extensively employed to enhance drug efficacy. In this study, salinomycin (SAL), a selective anti-CSC drug, and gemcitabine (GEM), a conventional anticancer drug, were co-loaded in liposomes and tested for optimal therapeutic efficacy. We employed the Design of Experiments approach to develop and optimize a liposomal delivery system for GEM and SAL. The antiproliferative effect of the liposomes was evaluated in SW-620 human colorectal cancer cells. The GEM and SAL-loaded liposomes exhibited adequate size, polydispersity, zeta potential, and drug content. The *in vitro* release study showed a sustained release of GEM and SAL from the liposomes over 72 h. Moreover, no sign of liposome aggregation was seen over 1 month and in a biological medium (FBS). The *in vitro* cytotoxic effects of the co-loaded liposomes were superior to that of single GEM either in free or liposomal form. The combination therapy using GEM and SAL co-loaded in liposomes could be a promising strategy for tackling colorectal cancer.

Hybrid Lipid Nanoformulations for Hepatoma Therapy: Sorafenib Loaded Nanoliposomes—A Preliminary Study (Nanomaterials, IF 5.719)

[2022]

A. Bartoș, I. Iancu*, L. Ciobanu, A. Onaciu, C. Moldovan,..., and R. Știufiuc*

Sorafenib is a multikinase inhibitor that has received increasing attention due to its high efficacy in hepatocellular carcinoma treatment. However, its poor pharmacokinetic properties (limited water solubility, rapid elimination, and metabolism) still represent major bottlenecks that need to be overcome in order to improve Sorafenib's clinical application. In this paper, we propose a nanotechnology-based hybrid formulation that has the potential to overcome these challenges: sorafenib-loaded nanoliposomes. Sorafenib molecules have been incorporated into the hydrophobic lipidic bilayer during the synthesis process of nanoliposomes using an original procedure developed in our laboratory and, to the best of our knowledge, this is the first paper reporting this type of analysis. The liposomal hybrid formulations have been characterized by transmission electron microscopy (TEM), dynamic light scattering (DLS), and nanoparticle tracking analysis (NTA) that provided useful information concerning their shape, size, zeta-potential, and concentration. The therapeutic efficacy of the nanohybrids has been evaluated on a normal cell line (LX2) and two hepatocarcinoma cell lines, SK-HEP-1 and HepG2, respectively.

Facile Microwave Assisted Synthesis of Silver Nanostars for Ultrasensitive Detection of Biological Analytes by SERS (International Journal of Molecular Sciences, IF 6.208)

[2022]

R. N. Revnic, G. F. Știufiuc, V. Toma, A. Onaciu, A. Moldovan,..., and R. Știufiuc*

We report a very simple, rapid and reproducible method for the fabrication of anisotropic silver nanostars (AgNS) that can be successfully used as highly efficient SERS substrates for different bioanalytes, even in the case of a near-infra-red (NIR) excitation laser. The nanostars have been synthesized using the chemical reduction of Ag+ ions by trisodium citrate. This is the first research reporting the synthesis of AgNS using only trisodium citrate as a reducing and stabilizing agent. The key elements of this original synthesis procedure are rapid hydrothermal synthesis of silver nanostars followed by a cooling down procedure by immersion in a water bath. The synthesis was performed in a sealed bottom flask homogenously heated and brought to a boil in a microwave oven. After 60 s, the colloidal solution was cooled down to room temperature by immersion in a water bath at 35 °C. The as-synthesized AgNS were washed by centrifugation and used for SERS analysis of test molecules (methylene blue) as well as biological analytes: pharmaceutical compounds with various Raman cross sections (doxorubicin, atenolol & metoprolol), cell lysates and amino acids (methionine & cysteine). UV-Vis absorption spectroscopy, (Scanning) Transmission Electron Microscopy ((S)TEM) and Atomic Force Microscopy (AFM) have been employed for investigating nanostars' physical properties.

New Insights into the Multivariate Analysis of SER Spectra Collected on Blood Samples for Prostate Cancer Detection: Towards a Better Understanding of the Role Played by Different Biomolecules on Cancer Screening: A Preliminary Study (Cancers, IF 6.575)

[2022]

V. C. Munteanu, R. A. Munteanu, D. Gulei, R. Mărginean, V. H. Schițcu,..., and R. Știufiuc*

It is possible to obtain diagnostically relevant data on the changes in biochemical elements brought on by cancer via the use of multivariate analysis of vibrational spectra recorded on biological fluids. Prostate cancer and control groups included in this research generated almost similar SERS spectra, which means that the values of

peak intensities present in SERS spectra can only give unspecific and limited information for distinguishing between the two groups. Our diagnostic algorithm for prostate cancer (PCa) differentiation was built using principal component analysis and linear discriminant analysis (PCA-LDA) analysis of spectral data, which has been widely used in spectral data management in many studies and has shown promising results so far. In order to fully utilize the entire SERS spectrum and automatically determine the most meaningful spectral features that can be used to differentiate PCa from healthy patients, we perform a multivariate analysis on both the entire and specific spectral intervals. Using the PCA-LDA model, the prostate cancer and control groups are clearly distinguished in our investigation. The separability of the following two data sets is also evaluated using two alternative discrimination techniques: principal least squares discriminant analysis (PLS-DA) and principal component analysis—support vector machine (PCA-SVM).

New Insights into the Magnetic Properties of CoFe2O4@SiO2@Au Magnetoplasmonic Nanoparticles (Nanomaterials, IF 5.719)

[2022]

R. Bortnic, A. Szatmari, G. Souca, R. Hirian, R. Dudric, L. Barbu-Tudoran, R. Știufiuc et al.

We report the successful synthesis and a complete magnetic characterization of CoFe2O4@SiO2@Au magnetoplasmonic nanoparticles. The CoFe2O4 magnetic nanoparticles were prepared using the hydrothermal method. A subsequent SiO2 shell followed by a plasmonic Au shell were deposited on the magnetic core creating magnetoplasmonic nanoparticles with a core–shell architecture. A spin-glass-type magnetism was shown at the surface of the CoFe2O4 nanograins. Depending on the external magnetic field, two types of spin-glass were identified and analyzed in correlation with the exchange field acting on octahedral and tetrahedral iron sites. The magnetization per formula unit of the CoFe2O4 core is not changed in the case of CoFe2O4@SiO2@Au nanocomposites. The gold nanoparticles creating the plasmonic shell show a giant diamagnetic susceptibility, dependent on their crystallite sizes.

Off-Resonance Gold Nanobone Films at Liquid Interface for SERS Applications (Sensors, IF 3.847)

[2021]

R. Moldovan, V. Toma, B. C. Iacob, R. Știufiuc, E. Bodoki*

Extensive effort and research are currently channeled towards the implementation of SERS (Surface Enhanced Raman Spectroscopy) as a standard analytical tool as it has undisputedly demonstrated a great potential for trace detection of various analytes. Novel and improved substrates are continuously reported in this regard. It is generally believed that plasmonic nanostructures with plasmon resonances close to the excitation wavelength (on-resonance) generate stronger SERS enhancements, but this finding is still under debate. In the current paper, we compared off-resonance gold nanobones (GNBs) with on-resonance GNBs and gold nanorods (GNRs) in both colloidal dispersion and as close-packed films self-assembled at liquid-liquid interface. Rhodamine 6G (R6G) was used as a Raman reporter in order to evaluate SERS performances. A 17-, 18-, and 55-fold increase in the Raman signal was observed for nanostructures (off-resonance GNBs, on-resonance GNBs, and on-resonance GNRs, respectively) assembled at liquid-liquid interface compared to the same nanostructures in colloidal dispersion. SERS performances of off-resonance GNBs were superior to on-resonance nanostructures in both cases. Furthermore, when off-resonance GNBs were assembled at the liquid interface, a relative standard deviation of 4.56% of the recorded signal intensity and a limit of detection (LOD) of 5 × 10−9 M could be obtained for R6G, rendering this substrate suitable for analytical applications.

The Effect of Zn-Substitution on the Morphological, Magnetic, Cytotoxic, and In Vitro Hyperthermia Properties of Polyhedral Ferrite Magnetic Nanoparticles (Pharmaceutics, IF 6.525)

[2021]

I. Fizeșan, C. Iacoviță, A. Pop, B. Kiss, R. Dudric,..., and R. Știufiuc*

The clinical translation of magnetic hyperthermia (MH) needs magnetic nanoparticles (MNPs) with enhanced heating properties and good biocompatibility. Many studies were devoted lately to the increase in the heating power of iron oxide MNPs by doping the magnetite structure with divalent cations. A series of MNPs with variable Zn/Fe molar ratios (between 1/10 and 1/1) were synthesized by using a high-temperature polyol method, and their physical properties were studied with different techniques (Transmission Electron Microscopy, X-ray diffraction, Fourier Transform Infrared Spectroscopy). At low Zn doping (Zn/Fe ratio 1/10), a significant increase in the saturation magnetization (90 e.m.u./g as compared to 83 e.m.u./g for their undoped counterparts) was obtained. The MNPs' hyperthermia properties were assessed in alternating magnetic fields up to 65 kA/m at a frequency of 355 kHz, revealing specific absorption rates of up to 820 W/g. The Zn ferrite MNPs showed good biocompatibility against two cell lines (A549 cancer cell line and BJ normal cell line) with a drop of only 40% in the

viability at the highest dose used (500 μg/cm2). Cellular uptake experiments revealed that the MNPs enter the cells in a dose-dependent manner with an almost 50% higher capacity of cancer cells to accommodate the MNPs. In vitro hyperthermia data performed on both cell lines indicate that the cancer cells are more sensitive to MH treatment with a 90% drop in viability after 30 min of MH treatment at 30 kA/m for a dose of 250 μg/cm2. Overall, our data indicate that Zn doping of iron oxide MNPs could be a reliable method to increase their hyperthermia efficiency in cancer cells.

Proving Nanoscale Chiral Interactions of Cyclodextrins and Propranolol Enantiomers by Means of SERS Measurements Performed on a Solid Plasmonic Substrate (Pharmaceutics, IF 6.525)

[2021]

G. F. Știufiuc, V. Toma, A. Onaciu, V. Chiș, C. M. Lucaciu, R. Știufiuc*

Chiral separation is an important issue for the pharmaceutical industry. Over the years, several separation methods have been developed, mainly based on chromatography. Their working principle is based on the formation of transient diastereoisomers, but the very subtle nanoscale interactions responsible for separation are not always understood. Recently, Raman and surface-enhanced Raman (SERS) spectroscopy have provided promising results in this field. Here we present Raman/SERS experimental data that provide useful information concerning the nanoscale interactions between propranolol enantiomers and α, β, and γ cyclodextrins. Raman spectroscopy was used to prove the formation of host–guest intermolecular complexes having different geometries of interaction. The occurrence of new vibrational bands and a change in the intensities of others are direct proofs of complexes' formation. These observations were confirmed by DFT calculations. By performing SERS measurements on a new type of plasmonic substrate, we were able to prove the intermolecular interactions responsible for PRNL discrimination. It turned out that the interaction strength between the substrate and the intermolecular complexes is of paramount importance for SERS-based chiral discrimination. This approach could represent a very good starting point for the evaluation of molecular interactions manifesting between other pharmaceutical compounds and different classes of chiral selectors.

Quantifying Cytosolic Cytochrome c Concentration Using Carbon Quantum Dots as a Powerful Method for Apoptosis Detection (Pharmaceutics, IF 6.525)

[2021]

C.S. Moldovan, A. Onaciu, V. Toma, R. Mărginean, A. Moldovan,..., and R. Știufiuc*

Background: Cytochrome c (Cyt c) is a key biomarker for early apoptosis, and many methods were designed to detect its release from mitochondria. For a proper evaluation of these programed cell death mechanisms, fluorescent nanoparticles are excellent candidates due to their valuable optical properties. Among all classes of nanoparticles developed thus far, carbon-based quantum dots bring qualitative and efficient imaging strategies for biomedical applications as a consequence of their biocompatibility and low cytotoxicity. Methods: In this study, we synthesized carbon quantum dots smaller than 5 nm from sodium citrate and polyethylene imine. These nanoparticles were rigorously characterized, and their quenching capacity in apoptotic events was assessed in A549 cells treated with staurosporine and etoposide. For the evaluation of Cyt c release, a phenomenon directly correlated with apoptotic events, we ran a semiquantitative analysis using confocal laser scanning microscopy. Results: Carbon quantum dots were synthesized and were successfully employed for Cyt c detection by means of fluorescence microscopy. Significant drops in fluorescence intensity were observed in the case of cells treated with apoptosis-inducing therapeutic compounds compared to untreated cells, confirming Cyt c release from mitochondria to cytosol. Conclusion: Considering these results, we strongly believe this method can contribute to an indirect in vitro evaluation of apoptosis.

A Screening Study for the Development of Simvastatin-Doxorubicin Liposomes, a Co-Formulation with Future Perspectives in Colon Cancer Therapy (Pharmaceutics, IF 6.525)

[2021]

C. Barbălată, A. S. Porfire, A. Sesărman, V.F. Rauca, M. Banciu, D. Muntean, R. Știufiuc et al.

An increasing number of studies published so far have evidenced the benefits of Simvastatin (SIM) and Doxorubicin (DOX) co-treatment in colorectal cancer. In view of this, the current study aimed to investigate the pharmaceutical development of liposomes co-encapsulating SIM and DOX, by implementing the Quality by Design (QbD) concept, as a means to enhance the antiproliferative effect of the co-formulation on C26 murine colon cancer cells co-cultured with macrophages. It is known that the quality profile of liposomes is dependent on the critical quality attributes (CQAs) of liposomes (drug entrapped concentration, encapsulation efficiency, size, zeta potential, and drug release profile), which are, in turn, directly influenced by various formulation factors and processing parameters. By using the design of experiments, it was possible to outline the increased variability of

CQAs in relation to formulation factors and identify by means of statistical analysis the material attributes that are critical (phospholipids, DOX and SIM concentration) for the quality of the co-formulation. The in vitro studies performed on a murine colon cancer cell line highlighted the importance of delivering the optimal drug ratio at the target site, since the balance antiproliferative vs. pro-proliferative effects can easily be shifted when the molar ratio between DOX and SIM changes.

Applying The Principles Of Quality By Design (QbD) Coupled With Multivariate Data Analysis (MVDA) In Establishing The Impact Of Raw Material Variability For Extended Release Tablets (Farmacia, IF 1.550)

[2021]

K. Ilies, T. Casian, D. Hales, G. Borodi, L. Rus, R. Știufiuc, I. Tomuța

The raw material is acknowledged to be a source of variability, however, the conventional, empirical development approach does not offer much information regarding its critical attributes and how processes can be modulated to remain in the constant quality region of the product. The study aimed to develop extended release hydrophilic matrix tablets with indapamide based on the Quality by Design (QbD) concept, evaluating the impact of interchanging different types and suppliers of raw material on the finished product quality profile. Results showed significant in vitro release test variability, with 16 - 71% failure rates when compared to four different EMA and FDA dissolution specification recommendations. Design of experiments based impact assessment concluded that the active pharmaceutical ingredient, hydroxypropyl methylcellulose and compression force was accountable for the variation, while orthogonal partial least squares (O2PLS) based root cause analysis extension redefined results in term of critical material attributes. Findings suggest that a risk-based, multivariate analysis assisted control strategy for the incoming raw materials could prevent quality concerns within routine manufacturing.

Testing the Limits of a Portable NIR Spectrometer: Content Uniformity of Complex Powder Mixtures Followed by Calibration Transfer for In-Line Blend Monitoring (Molecules, IF 4.927)

[2021]

T. Casian, A. Găvan, S. Iurian, A. Porfire, V. Toma, R. Știufiuc

(1) Background: Portable NIR spectrometers gain more and more ground in the field of Process Analytical Technology due to the easy on-site flexibility and interfacing versatility. These advantages that originate from the instrument miniaturization, also come with a downside with respect to performance compared to benchtop devices. The objective of this work was to evaluate the performance of MicroNIR in a pharmaceutical powder blend application, having three active ingredients and 5 excipients. (2) Methods: Spectral data was recorded in reflectance mode using static and dynamic acquisition, on calibration set samples developed using an experimental design. (3) Results: The developed method accurately predicted the content uniformity of these complex mixtures, moreover it was validated in the entire calibration range using ±10% acceptance limits. With respect to at-line prediction, the method presented lower performance compared to a previously studied benchtop spectrometer. Regarding the in-line monitoring of the blending process, it was shown that the spectral variability-induced by dynamic acquisition could be efficiently managed using spectral pre-processing. (4) Conclusions: The in-line process monitoring resulted in accurate concentration profiles, highlighting differences in the mixing behaviour of the investigated ingredients. For the low dose component homogeneity was not reached due to an inefficient dispersive mixing.

Percutaneous ultrasound guided PEG-coated gold nanoparticles enhanced radiofrequency ablation in liver (Scientific reports, IF 4.997)

[2021]

T. Mocan, R. Știufiuc, C. Popa, I. Nenu, Cosmin Peștean, A. L. Nagy et al.

To investigate the effects of PEG-coated gold nanoparticles on ablation zone volumes following in vivo radiofrequency ablation of porcine liver. This prospective study was performed following institutional animal care and committee approval was used. Radiofrequency ablations were performed in the livers of ten Sus scrofa domesticus swines. During each ablation, 10 mL (mL) of Peg-coated gold nanoparticles at two different concentrations (0.5 mg/mL and 0.01 mg/mL) were injected through the electrode channel into the target zone. For the control group, 10 mL of physiological saline was used. Five to ten minutes after each ablation, contrast enhanced ultrasound (CEUS) was performed to evaluate the volume of the coagulation zone. On day five we performed another CEUS and the animals were sacrificed. Treated tissues were explanted for quantification of the ablation zones' volumes. Hematoxylin and eosin (H&E) staining was also performed for histologic analysis. A total of 30 ablations were performed in the livers. The mean coagulation zone volume as measured by CEUS on

day 5 after RFA was: 21.69 ± 3.39 cm3, 19.22 ± 5.77 cm3, and 8.80 ± 3.33 cm3 for N1, N2 and PS respectively. The coagulation zone volume after N1 and N2 treatments was significantly higher compared to PS treatment ($p < 0.001$ and $p = 0.025$ respectively). There was no difference between N1 and N2 treatment ($p = 0.60$). In our proof-of concept, pilot study we have shown for the first time that when injected directly into the target tissue during RFA, gold nanoparticles can substantially increase the coagulation zone.

Surface-enhanced Raman scattering for the diagnosis of ulcerative colitis: will it change the rules of the game? (Analytical and Bioanalytical Chemistry, IF 3.286)

[2021]

C. Tefas*, R. Mărginean, V. Toma, B. Petrushev, P. Fischer, M. Tanțău, R. Știufiuc

Ulcerative colitis (UC) is a relapsing-remitting inflammatory bowel disease that requires numerous costly invasive investigations which lead to physical and psychological patient discomfort. We need a non-invasive technological approach that would significantly improve its diagnosis. Surface-enhanced Raman scattering (SERS) is a growing technique that can provide a molecular diagnostic fingerprint in just a few minutes, without the need for prior sample preparation. The aim of this pilot in vivo study was to prove that multivariate analysis of SER spectra collected on plasma samples could be employed for non-invasive diagnosis of UC. Plasma samples were collected from healthy subjects ($n = 35$) and patients with UC ($n = 28$). SERS spectra were acquired using a 785-nm excitation laser line and a solid plasmonic substrate developed in our laboratory using an original procedure described in the literature. The classification accuracy yielded by SERS was assessed by principal component analysis-linear discriminant analysis (PCA-LDA) and partial least squares discriminant analysis (PLS-DA). PCA-LDA differentiated UC samples from those of healthy subjects with a sensitivity of 86%, a specificity of 92%, and an accuracy of 89%, the AUC being 0.96. The PLS-DA analysis resulted in a sensitivity of 89%, a specificity of 94%, an accuracy of 92%, and an AUC value of 0.92. Several spectral bands were associated with UC: 376–420, 440–513, 686–715, 919–939, 1035–1062, 1083–1093, 1120–1132, 1148–1156, 1191–1211, 1234–1262, 1275–1294, 1382–1405, 1511–1526, and 1693–1702 cm−1. Changes in plasma levels of amino acids, proteins, lipids, and other compounds were noted using SERS in patients with UC. Multivariate analysis of SER spectra collected on a solid plasmonic substrate represents a promising alternative to diagnosing UC, as it is non-invasive, easy to use, and fast.

Transforming growth factor beta-mediated micromechanics modulates disease progression in primary myelofibrosis (Journal of Cellular and Molecular Medicine, IF 5.31)

[2020]

P. Teodorescu, S. Pașca, A. Jurj, G. Gafencu, J. P. Joelsson, R. Știufiuc et al.

Primary myelofibrosis (PMF) is a Ph-negative myeloproliferative neoplasm (MPN), characterized by advanced bone marrow fibrosis and extramedullary haematopoiesis. The bone marrow fibrosis results from excessive proliferation of fibroblasts that are influenced by several cytokines in the microenvironment, of which transforming growth factor-β (TGF-β) is the most important. Micromechanics related to the niche has not yet been elucidated. In this study, we hypothesized that mechanical stress modulates TGF-β signalling leading to further activation and subsequent proliferation and invasion of bone marrow fibroblasts, thus showing the important role of micromechanics in the development and progression of PMF, both in the bone marrow and in extramedullary sites. Using three PMF-derived fibroblast cell lines and transforming growth factor-β receptor (TGFBR) 1 and 2 knock-down PMF-derived fibroblasts, we showed that mechanical stress does stimulate the collagen synthesis by the fibroblasts in patients with myelofibrosis, through the TGFBR1, which however seems to be activated through alternative pathways, other than TGFBR2.

Solid Plasmonic Substrates for Breast Cancer Detection by Means of SERS Analysis of Blood Plasma (Nanomaterials, IF 5.719)

[2020]

G. F. Știufiuc, V. Toma, M. Bușe, R. Mărginean, G. Morar-Bolba,..., and R. Știufiuc*

Surface enhanced Raman spectroscopy (SERS) represents a promising technique in providing specific molecular information that could have a major impact in biomedical applications, such as early cancer detection. SERS requires the presence of a suitable plasmonic substrate that can generate enhanced and reproducible diagnostic relevant spectra. In this paper, we propose a new approach for the synthesis of such a substrate, by using concentrated silver nanoparticles purified using the Tangential Flow Filtration method. The capacity of our substrates to generate reproducible and enhanced Raman signals, in a manner that can allow cancer detection by means of Multivariate Analysis (MVA) of Surface Enhanced Raman (SER) spectra, has been tested on blood plasma samples collected from 35 healthy donors and 29 breast cancer patients. All the spectra were analyzed by a combined Principal Component-Linear Discriminant Analysis. Our results facilitated the discrimination between

healthy donors and breast cancer patients with 90% sensitivity, 89% specificity and 89% accuracy. This is a direct consequence of substrates' ability to generate diagnostic relevant spectral information by performing SERS measurements on pristine blood plasma samples. Our results suggest that this type of solid substrate could be employed for the detection of other types of cancer or other diseases by means of MVA-SERS procedure.

Saturation of Specific Absorption Rate for Soft and Hard Spinel Ferrite Nanoparticles Synthesized by Polyol Process (Magnetochemistry, IF 3.336)

[2020]

C. Iacoviță, G. F. Știufiuc, R. Dudric, N. Vedeanu, R. Tetean, R. I. Știufiuc*, C. M. Lucaciu*

Spinel ferrite nanoparticles represent a class of magnetic nanoparticles (MNPs) with enormous potential in magnetic hyperthermia. In this study, we investigated the magnetic and heating properties of spinel soft $NiFe_2O_4$, $MnFe_2O_4$, and hard $CoFe_2O_4$ MNPs of comparable sizes (12–14 nm) synthesized by the polyol method. Similar to the hard ferrite, which predominantly is ferromagnetic at room temperature, the soft ferrite MNPs display a non-negligible coercivity (9–11 kA/m) arising from the strong interparticle interactions. The heating capabilities of ferrite MNPs were evaluated in aqueous media at concentrations between 4 and 1 mg/mL under alternating magnetic fields (AMF) amplitude from 5 to 65 kA/m at a constant frequency of 355 kHz. The hyperthermia data revealed that the SAR values deviate from the quadratic dependence on the AMF amplitude in all three cases in disagreement with the Linear Response Theory. Instead, the SAR values display a sigmoidal dependence on the AMF amplitude, with a maximum heating performance measured for the cobalt ferrites (1780 W/g_{Fe+Co}), followed by the manganese ferrites (835 W/g_{Fe+Mn}), while the nickel ferrites (540 W/g_{Fe+Ni}) present the lowest values of SAR. The heating performances of the ferrites are in agreement with their values of coercivity and saturation magnetization.

In Vitro Intracellular Hyperthermia of Iron Oxide Magnetic Nanoparticles, Synthesized at High Temperature by a Polyol Process (Pharmaceutics, IF 6.525)

[2020]

C. Iacoviță, I. Fizeșan, A. Pop, L. Scoruș, R. Dudric,..., and R. Știufiuc*

We report the synthesis of magnetite nanoparticles (IOMNPs) using the polyol method performed at elevated temperature (300 °C) and high pressure. The ferromagnetic polyhedral IOMNPs exhibited high saturation magnetizations at room temperature (83 emu/g) and a maximum specific absorption rate (SAR) of 2400 W/g_{Fe} in water. The uniform dispersion of IOMNPs in solid matrix led to a monotonous increase of SAR maximum (3600 W/g_{Fe}) as the concentration decreased. Cytotoxicity studies on two cell lines (cancer and normal) using Alamar Blues and Neutral Red assays revealed insignificant toxicity of the IOMNPs on the cells up to a concentration of 1000 μg/mL. The cells internalized the IOMNPs inside lysosomes in a dose-dependent manner, with higher amounts of IOMNPs in cancer cells. Intracellular hyperthermia experiments revealed a significant increase in the macroscopic temperatures of the IOMNPs loaded cell suspensions, which depend on the amount of internalized IOMNPs and the alternating magnetic field amplitude. The cancer cells were found to be more sensitive to the intracellular hyperthermia compared to the normal ones. For both cell lines, cells heated at the same macroscopic temperature presented lower viability at higher amplitudes of the alternating magnetic field, indicating the occurrence of mechanical or nanoscale heating effects.

Physical properties of Zn doped Fe3O4 nanoparticles (Journal of Optoelectronics and Advanced Materials, IF 0.587)

[2020]

G. Souca, R. Dudric, C. Iacoviță, A. Moldovan, T. Frențiu, R. Știufiuc et al.

Two series of octahedral Fe3-xZnxO4 nanoparticles with mean sizes of 27 nm and 73 nm were prepared by thermal decomposition. All samples crystallize in inverse spinel cubic type structure with the Zn2+ ions located in tetrahedral sites. Magnetic measurements indicate an increase of the saturation magnetizations by 20% for a Zn content of x=0.12. The estimated anisotropy constants are close to that of pure magnetite. The physical properties of the investigated series are analysed in correlation with their structural properties.

Development of BSA gel/Pectin/Chitosan polyelectrolyte complex microcapsules for Berberine delivery and evaluation of their inhibitory effect on Cutibacterium acnes (Reactive and Functional Polymers, IF 3.975)

[2020]

V. Pascalau, C. Bogdan, E. Pall, L. Matros, S.L. Pandea, M. Suciu, R. Stiufiuc et al.

The aim of this work was to develop a novel fully natural drug delivery system for the treatment of acne, based on core-shell microcapsules that contain Berberine (Brb). The two main objectives of the work were: a) the synthesis and the characterization of complex microcapsules (ms), ms encapsulating Berberine (ms-Brb), and b) *in vitro* evaluation of the release of Brb, of the cytotoxicity on normal skin cells and of the antimicrobial effect on *Cutibacterium acnes* (formerly *Propionibacterium acnes*) (*C. acnes*). For a), bovine serum albumin (BSA) gel-core microcapsules with alternating multilayer shells of calcium cross-linked Pectin (P) hydrogel and the polyelectrolyte complex formed by P and Chitosan (Chi) (BSA gel/P/Chi/P) were synthesized. The BSA gel-core microcapsules were obtained using a sacrificial $CaCO_3$ template method, while the multilayer shell was formed through a technique consisting in the layer-by-layer (Lbl) deposition of polyelectrolyte complex formed by P and Chi. Brb was encapsulated into the resulting microcapsules, by a process of diffusion from solution. The structure characterization of ms/ms-Brb was performed by FTIR and UV–Vis spectroscopy, X-ray diffraction, confocal laser scanning microscopy, and scanning electron microscopy. The *in vitro* assessment of ms/ms-Brb cytotoxicity on skin cells was performed using keratinocyte (HaCaT) cell line. Results of physicochemical analyses confirm the successful encapsulation of Brb in ms, and the *in vitro* biological study recommends ms-Brb as a candidate for future *in vivo* research targeting anti-acne treatment.

Magnetite nanoparticles for medical applications (AIP Conference Proceedings, IF 0.402)

[2020]

R. Dudric, G. Souca, A. Szatmari, T. Szilard, S. Nițică, R. Știufiuc et al.

Magnetite nanoparticles with 15-30 nm average sizes were prepared by thermal decomposition. Their crystal structures and morphology were analyzed in correlation with the magnetic properties. Magnetic features, characteristic to Verwey transition were shown. The magnetizations and coercive fields increase parallelly with the nanoparticles sizes.

Hyperthermia, Cytotoxicity, and Cellular Uptake Properties of Manganese and Zinc Ferrite Magnetic Nanoparticles Synthesized by a Polyol-Mediated Process (Nanomaterials, IF 5.719)

[2019]

C. Iacoviță, A. Florea, L. Scoruș, E. Pall, R. Dudric, R. Știufiuc et al.

Manganese and zinc ferrite magnetic nanoparticles (MNPs) were successfully synthesized using the polyol method in ethylene glycol and were found to have high saturation magnetization values (90–95 emu/g at 4 K) when formed by ~30-nm crystallites assembled in an ~80-nm multicore structure. Hyperthermia data revealed a sigmoidal dependence of the specific absorption rate (SAR) on the alternating magnetic field (AMF) amplitude, with remarkable saturation SAR values in water of ~1200 W/g_{Fe+Mn} and ~800 W/g_{Fe+Zn} for the Mn and Zn ferrites, respectively. The immobilization of the MNPs in a solid matrix reduced the maximum SAR values by ~300 $W/g_{Fe+Mn, Zn}$ for both ferrites. The alignment of the MNPs in a uniform static magnetic field, before their immobilization in a solid matrix, significantly increased their heating performance. Toxicity assays performed in four cell lines revealed a lower toxicity for the Mn ferrites, while in the case of the Zn ferrites, only ~50% of cells were viable upon their incubation for 24 h with 0.2 mg/mL of MNPs. Cellular uptake experiments revealed that both MNPs entered the cells in a time-dependent manner, as they were found initially in endosomes and later in the cytosol. All of the studied cell lines were more sensitive to the $ZnFe_2O_4$ MNPs.

Electrospun amorphous solid dispersions of meloxicam: Influence of polymer type and downstream processing to orodispersible dosage forms (International Journal of Pharmaceutics, IF 6.51)

[2019]

T. Casian, E. Borbás, K. Ilyés, B. Démuth, A. Farkas, R. Știufiuc et al.

The objectives of this work were to develop meloxicam based amorphous solid dispersion through electrospinning technique and evaluate the effect of the polymeric matrix on the physicochemical properties of the fibers and the downstream processing ability to orodispersible dosage forms. Drug – polymer interactions formed between Eudragit E and meloxicam, confirmed through Raman and 1HNMR spectra, enabled the development of fibers from ethanol, thus allowing an increased production rate compared to PVPk30 where a DMF:THF solvent system was suitable. Microflux dissolution-permeation studies showed a significantly higher diffusion from amorphous solid dispersions compared to crystalline meloxicam. The flux through the membrane was influenced by the polymers only under basic conditions, where the precipitation of Eudragit E limited the complete resolubilization of the active ingredient. This phenomenon was not observed during large volume

conventional dissolution testing. The effect of formulation on long term stability could not be highlighted as all products were stable up to 15 months, stored in closed holders at 25 °C ± 2 °C and 50%RH ± 10%. The increased surface area of fibers enabled tablet preparation with low pressures due to favorable bonding between particles during compression. PVPk30 formulation presented higher tabletability and compactability, as higher tensile strength compacts could be prepared. Eudragit E formulation had lower detachment and ejection stress, suggesting a lower sticking tendency during tableting. The presence of HPßCD in PVPk30 formulation offered improved morphological features of the fibers, however no significant effect was observed on dissolution, permeation or mechanical properties. Downstream processing was guided by polymer mechanical properties and solubility, thus PVPk30 fibers could be delivered in the form of orodispersible webs and conventional tablets, whereas Eudragit E fibers as orodispersible tablets.

XPS on Nd0.6-Bi Sr0.4MnO3 nano powders (Applied Surface Science, IF 7.392)

[2019]

R. Dudric, R. Bortnic, G. Souca, R. Ciceo-Lucacel, R. Știufiuc, R. Tetean

The structural and electronic properties on Nd0.6-xBixSr0.4MnO3 nano powders with x = 0, 0.05 and 0.1 are reported. The compounds were prepared using sol-gel combustion method. X-ray diffraction studies confirm that all samples crystallize in orthorhombic structure having Pnma space group. The powders consist of spherical particles that tend to agglomerate, with average grain sizes of about 40–50 nm. XPS measurements reveal a shift toward lower binding energies of Mn 3s, Mn 2p, Nd 3d, and O 1s core levels with increasing Bi content, which can be explained by the larger 'c' lattice parameter and therefore larger atomic distances. The analysis of the core level XPS spectra proves the existence of both Mn4+ and Mn3+ ions in all samples, as well as the localization of Bi3+ ions in the perovskite lattice. The XPS valence-band is dominated by extensively hybridized Nd 4f-O 2p states, with contributions from Mn 3d-O 2p bonding and Mn 3d states.

Development of a new fiberglass reinforced composite for Computer Assisted Design - Computer Aided Manufacturing applications in dentistry (Revista Materiale Plastice, IF 0.782)

[2019]

B. Culic, M. Varvara, R. Știufiuc, V. Toma, C. Culic, D. Prodan et al.

The aim of this work was the development of a series of glass fiber reinforced composites (FRCs) for CAD/ CAM applications in dentistry and the characterization of their structure by SEM, Raman and FTIR spectroscopy. A selection of 2 different types of resins (R1 composed from 25%Bis-GMA, 40%UEDMA, 35% DMTEG and R2 composed from 65%Bis-GMA, 35% DMTEG) with 2 different types of hybrid filler (F1 with 42% quartz, 42% radiopaque glass and 16 % hydroxyapatite and F2 with 90% quartz and 10% colloidal silica) and 3 different types of E type fiber glass geometries (veil 30g/m2 , twill 163g/m2 and textile 300g/m2) in 4, 6, 8 and 10 layers were used in this in vitro study. Raman analysis, showed a powerful interaction between the polymer and the fiber glass. FTIR and SEM data revealed that the different fiber glass geometries were well incorporated inside the resin, resulting an acceptable homogeneity. Within the limitation of this study, it is possible to achieve a fiber glass reinforced composite for the use of CAD/CAM technology. Further investigation must be done in order to test all the properties of the new material

The Effects of Low-Dose Irradiation on Human Saliva: A Surface-Enhanced Raman Spectroscopy Study (Diagnostics, IF 3.992)

[2019]

I. M. Colceriu-Șimon, M. Hedeșiu, V. Toma, G. Armencea, A. Moldovan,..., and R. Știufiuc*

Biological effects of low-dose ionizing radiation (IR) have been unclear until now. Saliva, because of the ease of collection, could be valuable in studying low-dose IR effects by means of surface-enhanced Raman spectroscopy (SERS). The objective of our study was to compare the salivary SER spectra recorded before and after low-dose IR exposure in the case of pediatric patients (PP). Unstimulated saliva was collected from ten PP before and after irradiation with a cone beam computed tomography (CBCT) machine used for diagnostic purposes. The SERS measurements have been recorded on dried saliva samples using a solid nanosilver plasmonic substrate synthesized using an original method developed in our laboratory. The experimental results showed that salivary SER spectra are dominated by three vibrational bands (441,735 and 2107 cm^{-1}) that can be assigned to bending and stretching vibrations of salivary thiocyanate (SCN-). After exposure, an immediate increase of vibrational bands assigned to SCN- has been recorded in the case of all samples, probably as a result of IR interaction with oral cavity. This finding suggests that SCN- could be used as a valuable biomarker for the detection and identification of low-dose radiation effects.

Gold nanorods: from anisotropy to opportunity. An evolution update (Nanomedicine, IF 4.727)

[2019]

A. Onaciu, C. Braicu, A-A. Zimța, A. Moldovan, R. Știufiuc, M. Bușe et al.

Gold nanoparticles have drawn attention to nanomedicine for many years due to their physicochemical properties, which include: good stability; biocompatibility; easy surface chemistry and superior magnetic; and last, electronic properties. All of these properties distinguish gold nanoparticles as advantageous carriers to be exploited. The challenge to develop new gold nanostructures has led to anisotropy, a new property to exploit for various medical applications: diagnostic and imaging strategies as well as therapeutic options. Gold nanorods are the most studied anisotropic gold nanoparticles because of the presence of two absorption peaks according to their longitudinal and transversal plasmon resonances. The longitudinal surface plasmonic resonance can provide the absorption in the near-infrared region and this is an important aspect of using gold nanorods for medical purposes.

SERS-based differential diagnosis between multiple solid malignancies: breast, colorectal, lung, ovarian and oral cancer (International Journal of Nanomedicine, IF 4.471)

[2019]

V. Moisoiu, A. Stefancu, D. Gulei, R. Boitor, L. Magdo, R. Știufiuc et al.

Purpose: Surface-enhanced Raman scattering (SERS) spectroscopy on serum and other biofluids for cancer diagnosis represents an emerging field, which has shown promising preliminary results in several types of malignancies. The purpose of this study was to demonstrate that SERS spectroscopy on serum can be employed for the differential diagnosis between five of the leading malignancies, ie, breast, colorectal, lung, ovarian and oral cancer.

Patients and methods: Serum samples were acquired from healthy volunteers (n=39) and from patients diagnosed with breast (n=42), colorectal (n=109), lung (n=33), oral (n=17), and ovarian cancer (n=13), comprising n=253 samples in total. SERS spectra were acquired using a 532 nm laser line as excitation source, while the SERS substrates were represented by Ag nanoparticles synthesized by reduction with hydroxylamine. The classification accuracy yielded by SERS was assessed by principal component analysis–linear discriminant analysis (PCA-LDA).

Results: The sensitivity and specificity in discriminating between cancer patients and controls was 98% and 91%, respectively. Cancer samples were correctly assigned to their corresponding cancer types with an accuracy of 88% for oral cancer, 86% for colorectal cancer, 80% for ovarian cancer, 76% for breast cancer and 59% for lung cancer.

Conclusion: SERS on serum represents a promising strategy of diagnosing cancer which can discriminate between cancer patients and controls, as well as between cancer types such as breast, colorectal, lung ovarian and oral cancer.

A novel label free electrochemical magnetoimmunosensor for human Interleukin-6 quantification in serum (Electroanalysis, IF 3.077)

[2019]

M. Tertiș, G. Melinte, B. Ciui, I. Șimon, R. Știufiuc, R. Săndulescu, C. Cristea

A novel magnetoimmunosensor, designed for sensitive and selective quantification of interleukin 6, is herein reported. The experimental design involves the covalent immobilization of anti-interleukin 6 antibody through an amidic bond formed with the carboxyl functionalities provided at the surface of protein G-functionalized magnetic microparticles, assuring a sandwich-type immunoassay with electrochemical label free detection. All the experimental parameters involved in the elaboration and testing protocol were optimized. A linear calibration plot between the charge transfer resistance and the logarithmic concentration of interleukin-6 was achieved in the 1 pg mL−1 to 1 μg mL−1 range. A limit of quantification of 1 pg mL−1 and a detection limit of 0.3 pg mL−1 were obtained. The optimized magnetoimmunosensor showed an excellent selectivity against some potentially interfering proteins and has been successfully applied for the determination of target protein in human serum, proving its clinical relevance.

Synergistical Use of Electrostatic and Hydrophobic Interactions for the Synthesis of a New Class of Multifunctional Nanohybrids: Plasmonic Magneto-Liposomes (Nanomaterials, IF 5.719)

[2019]

G. Știufiuc, S. Nițică, V. Toma, C. Iacoviță, D. Zahn, R. Tetean,..., and R. Știufiuc*

By carefully controlling the electrostatic interactions between cationic liposomes, which already incorporate magnetic nanoparticles in the bilayers, and anionic gold nanoparticles, a new class of versatile multifunctional nanohybrids (plasmonic magneto-liposomes) that could have a major impact in drug delivery and controlled release applications has been synthesized. The experimental results confirmed the successful synthesis of hydrophobic superparamagnetic iron oxide nanoparticles (SPIONs) and polyethylene glycol functionalized (PEGylated) gold nanoparticles (AuNPs). The SPIONs were incorporated in the liposomal lipidic bilayers, thus promoting the formation of cationic magnetoliposomes. Different concentrations of SPIONs were loaded in the membrane. The cationic magnetoliposomes were decorated with anionic PEGylated gold nanoparticles using electrostatic interactions. The successful incorporation of SPIONs together with the modifications they generate in the bilayer were analyzed using Raman spectroscopy. The plasmonic properties of the multifunctional nanohybrids were investigated using UV-Vis absorption and (surface-enhanced) Raman spectroscopy. Their hyperthermic properties were recorded at different frequencies and magnetic field intensities. After the synthesis, the nanosystems were extensively characterized in order to properly evaluate their potential use in drug delivery applications and controlled release as a result of the interaction with an external stimulus, such as an NIR laser or alternating magnetic field.

In vitro study of BSA gel/polyelectrolite complexes of core shell microcapsules encapsulating doxorubicin for antitumoral targeted treatement (International Journal of Polymeric Materials and Polymeric Biomaterials, IF 2.604)

[2019]

V. Paşcalău, E. Pall, M. Tertis, M. Suciu, C. Cristea, R. Știufiuc et al.

The aim of this study is to develop core shell microcapsules of bovine serum albumin (BSA) gel with a complex polyelectrolite multilayer shell of natural polysaccharides with opposite charges, pectin (P), chitosan (Chi), and hyaluronic acid (HA) respectively, encapsulating Doxorubicin (Dox) as a carrier for targeted anti-tumoral treatment of hepatic cell carcinoma (HCC). A sacrificial CaCO3 template method was used in order to obtain microcapsules with a BSA gel core and a layer-by-layer (Lbl) deposition technique of polyelectrolite complexes formed between P/Chi in the inner layers and HA/Chi in the outer shell layers. The preformed microcapsules, BSA gel/P/Chi/HA, noted as ms, have been applied for Dox encapsulation (ms-Dox). Dox encapsulation and release in different pH media were studied in order to elucidate the interactions between pH dependently charged species involved in the Dox loading/releasing processes. The structure characterization of ms/ms-Dox was evaluated by FTIR and UV-Vis spectroscopy, X-ray diffraction, thermal analy sis, optical microscopy, confocal laser scanning microscopy, and scanning electron microscopy. The *in vitro* study for citotoxicity assessment on normal and tumoral cells of both ms and ms-Dox was performed using mesenchymal stem cells (MSCs) and Hep2G HCC cell lines. Results of physical-chemical analyses confirm the successful encapsulation of Dox in ms, and the *in vitro* bio logical study recommends ms-Dox as a candidate for future *in vivo* research as a targeted anti-tumoral treatment modality applications.

PEGylated gold nanoparticles with intersting plasmonic properties synthesized using an original, rapid and easy to implement procedure (Journal of Nanomaterials, IF 2.986)

[2018]

Ș. Nițică, A. Moldovan, V. Toma, C. Moldovan, I. Berindan-Neagoe, R. Știufiuc et al.

In this letter, we report a new, one-step, rapid, and easy-to-implement method for the synthesis of PEGylated gold nanoparticles (PEG-AuNPs) having a narrow size distribution and very interesting plasmonic properties. Unmodified polyethylene glycol molecules with a molecular weight of 1000 g/mole (PEG1000) have been employed as reducing and capping agents for the synthesis of spherical gold nanoparticles having an average diameter of 35 nm, within a few minutes. The novelty of the herein proposed synthesis method consists in the fact that the synthesis takes place inside of a sealed bottle flask containing aqueous solutions of PEG1000, tetrachloroauric(III) acid (HAuCl4), and NaOH, placed in the center of a microwave oven, capable to provide a very uniform temperature environment. It turned out that, during the very short synthesis procedure (2 minutes), PEG 1000 suffers an oxidative transformation in such a manner that its terminal alcohol groups (-CH2-OH) are transformed in carboxylate ones (-COO−). The as-synthesized PEG-AuNPs possess very interesting plasmonic properties allowing the detection of different molecules by means of SER spectroscopy performed either in liquid droplets or on solid spots. As a consequence of their unique plasmonic properties, the SER spectra acquired using this new class of nanoparticles on different molecules of interest (methylene blue, rhodamine 6G, doxorubicin, and 5-fluorouracil) are highly reproducible, making them ideal candidates for further use as SERS substrates.

Exosome-carried microRNA-based signature as a cellular trigger for the evolution of chronic lymphocytic leukemia into Richter syndrome (Critical Reviews in Clinical Laboratory Sciences, IF 4.677)

[2018]

A. Jurj, L. Pop, B. Petrushev, S. Pasca, D. Dima, R. Știufiuc et al.

Even if considered a cumulative and not a proliferative CD5+ B-cell neoplasm, chronic lymphocytic leukemia (CLL) has a proliferation rate higher than that recognized earlier, especially in the lymphoid tissues. Some patients with CLL develop a clinical syndrome entitled Richter syndrome (RS). Understanding CLL genetics and epigenetics may help to elucidate the molecular basics of the clinical heterogeneity of this type of malignancy. In the present project we aimed to identify a microRNA species that can predict the evolution of therapy-resistant CLL towards RS. In the first phase of our study, microRNA-19b was identified as a possible target, and in the second phase, we transfected three different CLL cell lines with microRNA-19b mimic and inhibitor and assessed the potential role on leukemia cells *in vitro*. The mechanism by which miR-19b acts were identified as the upregulation of Ki67 and downregulation of p53. This was further supported through RT-PCR and western blotting on CLL cell lines, as well as by next generation sequencing on two patients diagnosed with CLL that evolved into RS.

The silent healer: miR-205-5p upregulation inhibits epithelial to mesenchymal transition in colon cancer cells by indirectly up-regulating E-cadherin expression (Critical Reviews in Clinical Laboratory Sciences, IF 12.07)

[2018]

D. Gulei, L. Magdo, A. Jurj, L. Raduly, R. Cojocneanu-Petric, R. Știufiuc et al.

EMT represents the dominant program within advanced stages of colon cancer, where cells acquire migratory characteristics in order to invade secondary tissues and form metastasis. Where the majority of the therapeutic strategies are concentrated on the reduction of the tumor mass through different apoptotic mechanisms, the present study advocates an important role for miR-205-5p in impairment of colon cancer cells migration and restoration of the epithelial phenotype. Upon identification of a homogenous downregulated profile for miR-205-5p in colon adenocarcinoma patients, functional studies demonstrated that experimental upregulation of this sequence is able to significantly raise the levels of E-cadherin through direct inhibition of ZEB1. Moreover, the elevation in CDH1 expression was translated into functional parameters where cells lost their invasion and migratory characteristics and formed homogenous clusters through adhesion interactions. Survival analysis of colon adenocarcinoma patients revealed that low levels of miR-205-5p are associated with an unfavorable prognostic compared to those with increased expression, demonstrating the possible clinical utility of miR-205-5p replacement. Exogenous administration of miRNA mimics was not associated with significant changes in cell viability or inflammatory pathways. Therefore, the proposed strategy is aiming towards inhibition of metastasis and limitation of the tumor borders in advanced stages patients in order to prolong the survival time and to increase the efficiency of the current therapeutic strategies.

Origanum vulgare mediated green synthesis of biocompatible gold nanoparticles simultaneously possessing plasmonic, antioxidant and antimicrobial properties (International Journal of Nanomedicine, IF 4.471)

[2018]

D. Benedec, I. Oniga, F. Cuibus, B. Sevastre, G. Stiufiuc,..., and R. Știufiuc*

Purpose: The leaves and flowering stem of *Origanum vulgare* contain essential oils, flavonoids, phenolic acids and anthocyanins. We propose a new, simple, one-pot, *O. vulgare* extract (OVE) mediated green synthesis method of biocompatible gold nanoparticles (AuNPs) possessing improved antioxidant, antimicrobial and plasmonic properties.

Materials and methods: Different concentrations of OVEs were used to reduce gold ions and to synthetize biocompatible spherical AuNPs. Their morphology and physical properties have been investigated by means of transmission electron microscopy, ultraviolet–visible absorption spectroscopy, photon correlation spectroscopy and Fourier transform infrared spectroscopy, whereas their plasmonic properties have been tested using surface-enhanced Raman spectroscopy (SERS). The antioxidant properties of nanoparticles (NPs) have been evaluated by 2,2-diphenyl-1-picrylhydrazyl radical scavenging assay, and the antimicrobial tests were performed using the disk diffusion assay. Their cytotoxicity has been assessed by means of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay.

Results: The experimental results confirmed the successful synthesis of biocompatible, spherical, plasmonic NPs having a mean diameter of ~40 nm and an outstanding aqueous stability. This new class of NPs exhibits a very good antioxidant activity and presents interesting inhibitory effects against *Staphylococcus aureus* and *Candida albicans*. Due to their plasmonic properties, AuNPs are used as SERS substrates for the detection of a test molecule (methylene blue) up to a concentration of 10-7 M and a pharmaceutical compound (propranolol) in solution. Cytotoxicity assays revealed that AuNPs are better tolerated by normal human dermal fibroblast cells, while the melanoma cancer cells are more sensitive.

Conclusion: The biocompatible AuNPs synthetized using OVEs showed significant bactericidal and antimycotic activities, the most sensitive microorganisms being *S. aureus* and *C. albicans*, both commonly involved in various dermatological infections. Moreover, the significant antioxidant effect might recommend their use for protective and/or preventive effect in various skin inflammatory conditions, including the reduction in side effects in dermatological infections. Meanwhile, the as-synthesized biocompatible AuNPs can be successfully used as SERS substrates for the detection of pharmaceutical compounds in aqueous solutions.

Nanoparticles mediated chiral separation using SERS (ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY)

[2018]

R. Stiufiuc, V. Toma, A. Moldovan, G. Stiufiuc, V. Chis, M. Lucaciu

One pot microwave assisted synthesis of cyclodextrines capped spherical gold nanoparticles (Digest Journal of Nanomaterials and Biostructures, IF 0.693)

[2017]

G. Știufiuc, V. Toma, A. Moldovan, R. Știufiuc*, C. M. Lucaciu

In this letter we report a new, simple and very rapid method for the synthesis of monodispersed spherical gold nanoparticles (AuNPs) using as reducing and capping agents the three classes of natural cyclodextrins (alfa α-, beta β- and gamma γ-CDs). The as-synthesized nanoparticles are remarkably stable in aqueous solutions and possess very interesting plasmonic properties allowing the detection of low concentration of analyte molecules, using Surface Enhanced Raman Spectroscopy (SERS). The spherical cyclodextrin capped gold nanoparticles (α-, β- or γCD@AuNps) were prepared in a very short period of time (less than 10 minutes) by mixing the Au3+ solutions with aqueous solution of each class of the natural cyclodextrins, followed by a very short heat treatment (2 minutes) inside of a microwave oven. The UV-Vis absorption spectra, measured right after the synthesis, revealed the existence of a strong and narrow plasmonic peak in the visible region, suggesting the successful synthesis of monodispersed spherical gold nanoparticles. The TEM and DLS measurements confirmed the presence of spherical gold nanoparticles having a mean diameter of 20 nm (αCD@AuNPs) and 30 nm (βCD@AuNPs and γCD@AuNPs) respectively. The plasmonic properties of AuNPs have been evaluated by means of SERS measurements performed on aqueous solution and on dry samples, using a standard test molecule (methylene blue) as well as a pharmaceutical compound having a very low Raman cross section (atenolol).

Small versus large iron oxide magnetic nanoparticles: Hyperthermia and cell uptake properties (Molecules, IF 4.927)

[2016]

C. Iacoviță, A. Florea, R. Dudric, E. Pall, A. I. Moldovan, R. Tetean, R. Știufiuc*, C. M. Lucaciu*

Efficient use of magnetic hyperthermia in clinical cancer treatment requires biocompatible magnetic nanoparticles (MNPs), with improved heating capabilities. Small (~34 nm) and large (~270 nm) Fe_3O_4-MNPs were synthesized by means of a polyol method in polyethylene-glycol (PEG) and ethylene-glycol (EG), respectively. They were systematically investigated by means of X-ray diffraction, transmission electron microscopy and vibration sample magnetometry. Hyperthermia measurements showed that Specific Absorption Rate (SAR) dependence on the external alternating magnetic field amplitude (up to 65 kA/m, 355 kHz) presented a sigmoidal shape, with remarkable SAR saturation values of ~1400 W/g_{MNP} for the small monocrystalline MNPs and only 400 W/g_{MNP} for the large polycrystalline MNPs, in water. SAR values were slightly reduced in cell culture media, but decreased one order of magnitude in highly viscous PEG1000. Toxicity assays performed on four cell lines revealed almost no toxicity for the small MNPs and a very small level of toxicity for the large MNPs, up to a concentration of 0.2 mg/mL. Cellular uptake experiments revealed that both MNPs penetrated the cells through endocytosis, in a time dependent manner and escaped the endosomes with a faster kinetics for large MNPs. Biodegradation of large MNPs inside cells involved an all-or-nothing mechanism.

The Influence of Molecular Structure Modifications on Vibrational Properties of Some Beta Blockers: A Combined Raman and DFT Study (Journal of Spectroscopy, IF 1.75)

[2016]

A. Farcaș, C. Iacoviță, E. Vințeler, V. Chiș, R. Știufiuc*, C. M. Lucaciu

We report results of a systematic Raman, SERS, and DFT study on four beta blocking molecules: Atenolol, Metoprolol, Propranolol, and, for the first time reported in the literature, Bisoprolol. The choice of these molecules was motivated by the structural similarities between Atenolol, Bisoprolol, and Metoprolol on one hand and by their differences relative to Propranolol. The density functional theory (DFT) approach, using the B3LYP method at the 6-311+G(d,p) level of theory, has been employed for geometry optimization and vibration bands assignments. The obtained results highlight the major role played by the central aromatic ring whose vibrations dominate the Raman spectra in all compounds. While the phenyl group vibrations dominate the Raman spectrum in the case of Atenolol, Bisoprolol, and Metoprolol, the spectrum of Propranolol presents high intensity vibrations of the naphthyl group. SERS performed on gold and silver colloids, at various pH conditions, revealed a higher sensitivity for Propranolol detection. The pH dependence of the spectrum indicates that the studied beta blockers attach themselves to the metal nanoparticles in a protonated form. The molecular adsorption geometry on metal nanoparticles surface has been evaluated by using the experimental SER spectra and the quantum chemical calculations.

Synthesis of multifunctional magneto/plasmonic liposomes for drug delivery applications (ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY)

[2016]

R. Stiufiuc, C. Iacovita, G. Stiufiuc, S. Nitica, C. Lucaciu

Ultraviolet light assisted synthesis of magnetoplasmonic nanoparticles (Digest Journal of Nanomaterials and Biostructures , IF 0.693)

[2015]

C. Iacovita, G. Stiufiuc, A. Florea, R. Știufiuc*, and C. M. Lucaciu

We report a new photochemical method to produce water-dispersible core-shell iron-oxidegold nanoparticles (Fe3O4@Au NPs). The Fe3O4 magnetic nanoparticles (MNPs) prepared by using the oleic acid/oleylamine method, hydrophylized with tetramethylammonium hydroxide were capped with citrate anions. Gold coating was achieved by UV irradiation of Fe3O4 MNPs suspended in Au3+ solution. UV-VIS absorption spectra revealed the existence of a strong plasmonic peak, attributed to the Au shell, which red-shifts as a function of the shell thickness surrounding the magnetic core. TEM images revealed the presence of magneto-plasmonic NPs with core-shell architecture of different geometries. The plasmonic properties of the NPs have been evaluated by means of Surface Enhanced Raman Spectroscopy. The SER spectra of methylene blue (MB) obtained using the here reported magneto-plasmonic NPs as Raman substrates are very similar with those obtained using "classical" Ag and Au colloids.

Polyethylene Glycol-Mediated Synthesis of Cubic Iron Oxide Nanoparticles with High Heating Power (Nanoscale Research Letters, IF 4.703)

[2015]

C. Iacovita, R. Știufiuc*, T. Radu, A. Florea, G. Stiufiuc, AG. Dutu, et al.

Iron oxide magnetic nanoparticles (IOMNPs) have been successfully synthesized by means of solvothermal reduction method employing polyethylene glycol (PEG200) as a solvent. The as-synthesized IOMNPs are poly-dispersed, highly crystalline, and exhibit a cubic shape. The size of IOMNPs is strongly dependent on the reaction time and the ration between the amount of magnetic precursor and PEG200 used in the synthesis method. At low magnetic precursor/PEG200 ratio, the cubic IOMNPs coexist with polyhedral IOMNPs. The structure and morphology of the IOMNPs were thoroughly investigated by using a wide range of techniques: TEM, XRD, XPS, FTIR, and RAMAN. XPS analysis showed that the IOMNPs comprise a crystalline magnetite core bearing on the outer surface functional groups from PEG200 and acetate. The presence of physisorbed PEG200 on the IOMNP surface is faintly detected through FT-IR spectroscopy. The surface of IOMNPs undergoes oxidation into maghemite as proven by RAMAN spectroscopy and the occurrence of satellite peaks in the Fe2p XP spectra. The magnetic studies performed on powder show that the blocking temperature (TB) of IOMNPs is around 300 K displaying a coercive field in between 160 and 170 Oe. Below the TB, the field-cooled (FC) curves turn concave and describe a plateau indicating that strong magnetic dipole-dipole interactions are manifested in between IOMNPs. The specific absorption rate (SAR) values increase with decreasing nanoparticle concentrations for the

IOMNPs dispersed in water. The SAR dependence on the applied magnetic field, studied up to magnetic field amplitude of 60 kA/m, presents a sigmoid shape with saturation values up to 1700 W/g. By dispersing the IOMNPs in PEG600 (liquid) and PEG1000 (solid), it was found that the SAR values decrease by 50 or 75 %, indicating that the Brownian friction within the solvent was the main contributor to the heating power of IOMNPs.

A new class of pegylated plasmonic liposomes: synthesis and characterization (Journal of Colloid and Interface Science, IF 9.965)

[2015]

R. Știufiuc*, C. Iacovita, G. Stiufiuc, A. Florea, M. Achim, and C. M. Lucaciu

The multifunctional nanoobjects that can be controlled, manipulated and triggered using external stimuli represent very promising candidates for nanoscale therapeutic and diagnostic applications. In this study we report the successful synthesis and characterization of a new class of very stable multifunctional nanoobjects, containing cationic liposomes decorated with PEGylated gold nanoparticles (PEGAuNPs). The multifunctional hybrid nanoobjects (mHyNp) were prepared by taking advantage of the electrostatic interactions between small unilamelar cationic liposomes and negatively charged gold nanoparticles. The mHyNps have been investigated by UV–VIS absorption spectroscopy, Dynamic Light Scattering (DLS), Zeta Potential Measurements and Transmission Electron Microscopy (TEM). The TEM images clearly revealed the attachment of individual gold nanoparticles onto the spherical outer surface of the cationic liposomes which was also confirmed by DLS and UV–VIS data. Furthermore, the plasmonic properties of the hybrid complexes have been evaluated by using the Surface Enhanced Raman Spectroscopy (SERS) technique. It is shown that PEG mediated interaction between the liposomes and the gold nanoparticles enabled the recording of the SER spectra of the liposomes in aqueous environment, thus demonstrating the plasmonic properties of the hybrids.

Surface mediated chiral interactions between cyclodextrins and propranolol enantiomers: a SERS and DFT study (Physical Chemistry Chemical Physics, IF 3.676)

[2015]

R. Știufiuc*, C. Iacovita, G. Stiufiuc, E. Bodoki, V. Chis, and C. M. Lucaciu

The nanoparticles mediated enantioselective recognition of propranolol enantiomers through native cyclodextrin complexation has been investigated by using surface-enhanced Raman spectroscopy (SERS). The highly efficient chiral recognition mechanism is based on a synergistic interaction between spherical noble metal nanoparticles, propranolol enantiomers and native cyclodextrins (CDs). Amongst the native cyclodextrins, β-CD has the highest chiral recognition ability for propranolol enantiomers, due to its specific shape and cavity size, thus producing the largest difference between the recorded SERS spectra of the two hosted enantiomers. The molecular interaction mechanism responsible for enantioselectivity was furthermore proven by quantum chemical calculations based on density functional theory (DFT). The theoretical calculations and experimental SER spectra allowed the assignment of functional moieties involved in the chiral recognition mechanism. The most important factors governing the highly efficient chiral probing by SERS are the fundamentally different mechanism of interaction between the *R*- and *S*-enantiomers and β-CD and the strength of interaction between the nanoparticle surface and the two propranolol–CD complexes. The role of metallic nanoparticles in the enantioselective recognition process has been experimentally evaluated by using silver and gold nanoparticles as SERS substrates, given their ability to interact differently with the complexes. The viability of this new method for chiral discrimination has been demonstrated for both substrates and could open new avenues for these kinds of applications.

One-Step Synthesis of PEGylated Gold Nanoparticles with Tunable Surface Charge (Journal of Nanomaterials, IF 2.986)

[2013]

R. Știufiuc*, C. Iacovita, R. Nicoara, G. Stiufiuc, A. Florea, M. Achim, and C. M. Lucaciu

The present work reports a rapid, simple and efficient one-step synthesis and detailed characterisation of stable aqueous colloids of gold nanoparticles (AuNPs) coated with unmodified poly(ethylene)glycol (PEG) molecules of different molecular weights and surface charges. By mixing and heating aqueous solutions of PEG with variable molecular chain and gold(III) chloride hydrate (HAuCl4) in the presence of NaOH, we have successfully produced uniform colloidal 5 nm PEG coated AuNPs of spherical shape with tunable surface charge and an average diameter of 30 nm within a few minutes. It has been found out that PEGylated AuNPs provide optical enhancement of the characteristic vibrational bands of PEG molecules attached to the gold surface when they are excited with both visible (532 nm) and NIR (785 nm) laser lines. The surface enhanced Raman scattering (SERS) signal does not depend on the length of the PEG molecular chain enveloping the AuNPs, and the stability of the colloid is not affected by the addition of concentrated salt solution (0.1 M NaCl), thus suggesting their potential

use for *in vitro* and *in vivo* applications. Moreover, by gradually changing the chain length of the biopolymer, we were able to control nanoparticles' surface charge from −28 to −2 mV, without any modification of the Raman enhancement properties and of the colloidal stability.

SERS active silver colloids prepared by reduction of silver nitrate with short-chain polyethylene glycol (Nanoscale Research Letters, IF 4.703)

[2013]

R. Știufiuc*, C. Iacovita, CM. Lucaciu, G. Stiufiuc, AG. Dutu, C. Braescu and N. Leopold

We report a fast, one-step, facile, and green preparation method that yields very stable and biocompatible silver colloids that are highly active as surface-enhanced Raman spectroscopy (SERS) platforms that has a possible application in biomedicine. Reduction of silver nitrate has been carried out using polyethylene glycol (PEG) which acts as both reducing agent and stabilizer. It turned out that the -OH groups provided by the addition of NaOH represent a key element in the successful synthesis of PEG-coated silver nanoparticles (AgNPs). The as-obtained silver colloids have been characterized by UV-visible spectroscopy, transmission electron spectroscopy, and SERS using 532- and 633-nm laser lines on a dispersive Raman spectrometer. Several analytes as methylene blue, *p*-aminothiophenol, amoxicillin, and Cu(PAR)2 were used to prove SERS enhancement of the obtained silver colloid. It has been found that the PEGylated AgNPs provide SERS signals comparable to those achieved using classical hydroxylamine and citrate-reduced silver colloids, thus demonstrating the ability of this new method to prepare biocompatible silver colloids.

Adsorption geometry of propranolol enantiomers on silver nanoparticles (Journal of Molecular Structure, IF 3.841)

[2013]

R. Știufiuc*, C. Iacovita, CM Lucaciu, G. Stiufiuc, R. Nicoara, M. Oltean, V. Chis, E. Bodoki

In the present work we report an experimental and theoretical study on propranolol a widely used beta-blocking drug. Raman and Surface Enhanced Raman Spectroscopies (SERSs) have been employed for the detection of the molecular vibrations, while quantum chemical calculations based on density functional theory (DFT) have been used to determine the geometrical, energetic and vibrational characteristics of propranolol. Using a 785 nm laser line, the SERS spectra of the two propranolol enantiomers adsorbed on hydroxylamine reduced silver colloids have been measured in the 3–11 pH range. Based on DFT calculations performed at the B3LYP level of theory the FT-IR, Raman and SERS spectra of propranolol enantiomers were assigned. The adsorption geometry of both enantiomers onto the silver surface was predicted using the calculated molecular electrostatic potential (MEP) in association with data obtained from SERS.

Chiral recognition and quantification of propranolol enantiomers by surface enhanced Raman scattering through supramolecular interaction with betacyclodextrin (Talanta, IF 6.057)

[2012]

E. Bodoki, M. Oltean, A. Bodoki, R. Știufiuc*

A simple, fast and accurate method of chiral recognition and quantification of propranolol enantiomers by surface enhanced Raman scattering (SERS) and multivariate regression analysis through supramolecular interaction with β-cyclodextrin is reported. Computational chemistry served as a tool of elucidating the underlying mechanism of molecular interactions responsible for chiral discrimination. The influence of several factors (nature and concentration of chiral auxiliary, selector-selectand ratio, pH, interaction time, etc.) over the obtained SERS spectra was assessed, followed by the construction of the chemometric model with the optimized operational conditions. The performance of the obtained semi-empirical model was established using a validation set of pure enantiomers and its intended use was demonstrated by the assessment of the enantiomeric excess of propranolol in pharmaceutical formulations (tablets) without the need of tedious and expensive chiral separation. The obtained results were also confirmed by chiral high-performance liquid chromatography.

Enhanced laser thermal ablation for the in vitro treatment of liver cancer by specific delivery of multiwalled carbon nanotubes functionalized with human serum albumin (International Journal of Nanomedicine, IF 4.471)

[2011]

C. Iancu, L. Mocan, C. Bele, A. Orza, F. Tabaran, C. Catoi, R. Știufiuc et al.

The main goal of this investigation was to develop and test a new method of treatment for human hepatocellular carcinoma (HCC). We present a method of carbon nanotube-enhanced laser thermal ablation of HepG2 cells

(human hepatocellular liver carcinoma cell line) based on a simple multiwalled carbon nanotube (MWCNT) carrier system, such as human serum albumin (HSA), and demonstrate its selective therapeutic efficacy compared with normal hepatocyte cells. Both HepG2 cells and hepatocytes were treated with HSA-MWCNTs at various concentrations and at various incubation times and further irradiated using a 2 W, 808 nm laser beam. Transmission electron, phase contrast, and confocal microscopy combined with immunochemical staining were used to demonstrate the selective internalization of HSA-MWCNTs via Gp60 receptors and the caveolin-mediated endocytosis inside HepG2 cells. The postirradiation apoptotic rate of HepG2 cells treated with HSA-MWCNTs ranged from 88.24% (for 50 mg/L) at 60 sec to 92.34% (for 50 mg/L) at 30 min. Significantly lower necrotic rates were obtained when human hepatocytes were treated with HSA-MWCNTs in a similar manner. Our results clearly show that HSA-MWCNTs selectively attach on the albondin (aka Gp60) receptor located on the HepG2 membrane, followed by an uptake through a caveolin-dependent endocytosis process. These unique results may represent a major step in liver cancer treatment using nanolocalized thermal ablation by laser heating.

Selective ex-vivo photothermal ablation of human pancreatic cancer with albumin functionalized multiwalled carbon nanotubes (International Journal of Nanomedicine, IF 4.471)

[2011]

L. Mocan, F. Tabaran, T. Mocan, C. Bele, A. Orza, C. Lucan, R. Știufiuc, et al.

The process of laser-mediated ablation of cancer cells marked with biofunctionalized carbon nanotubes is frequently called "nanophotothermolysis". We herein present a method of selective nanophotothermolisys of pancreatic cancer (PC) using multiwalled carbon nanotubes (MWCNTs) functionalized with human serum albumin (HSA). With the purpose of testing the therapeutic value of these nanobioconjugates, we have developed an ex-vivo experimental platform. Surgically resected specimens from patients with PC were preserved in a cold medium and kept alive via intra-arterial perfusion. Additionally, the HSA-MWCNTs have been intra-arterially administered in the greater pancreatic artery under ultrasound guidance. Confocal and transmission electron microscopy combined with immunohistochemical staining have confirmed the selective accumulation of HSA-MWCNTs inside the human PC tissue. The external laser irradiation of the specimen has significantly produced extensive necrosis of the malign tissue after the intra-arterial administration of HSA-MWCNTs, without any harmful effects on the surrounding healthy parenchyma. We have obtained a selective photothermal ablation of the malign tissue based on the selective internalization of MWCNTs with HSA cargo inside the pancreatic adenocarcinoma after the ex-vivo intra-arterial perfusion.

Anisotropic Gold Nanocrystals: synthesis and characterization (International Journal of Modern Physics B, IF 1.219)

[2010]

R. Știufiuc, F. Toderas, M. Iosin, G. Știufiuc

In this letter we report on successful preparation and characterization of anisotropic gold nanocrystals bio-synthesized by reduction of aqueous chloroaurate ions in pelargonium plant extract. The nanocrystals have been characterized by means of Transmission Electron Microscopy (TEM), UV-VIS absorption spectroscopy and tapping mode atomic force microscopy (TM-AFM). Using these investigation techniques, the successful formation of anisotropic single nanocrystals with the preferential growth direction along the gold (111) plane has been confirmed. The high detail phase images could give us an explanation concerning the growth mechanism of the nanocrystals.

Above-barrier surface electron resonances induced by a molecular network (PHYSICAL REVIEW B, IF 3.908)

[2010]

R. Știufiuc, L. M. A. Perdigão , B. Grandidier, D. Deresmes, G. Allan, C. Delerue, et al.

We report the modification of the density of states of the Ag/Si(111)-root 3 X root 3R30 degrees surface by a self-assembled molecular network at energies much higher than the height of the potential barriers induced by the molecules. Map of the differential conductance obtained by scanning tunneling spectroscopy reveals an increase in the electron density in the pores of the network. This enhanced electronic resonance is explained by theoretical calculations where the periodic potential introduced by the molecular network causes band replica with an alteration of the surface band structure.

Vibrational and electronic structure of PTCDI and melamine-PTCDI complexes (Journal of Molecular Structure, IF 3.841)

[2009]

V. Chis, G. Mile, R. Știufiuc, N. Leopold, M. Oltean

Vibrational FT-IR, FT-IR/ATR and Raman spectra of 3,4,9,10-perylene-tetracarboxylic diimide (PTCDI) and 1,3,5-triazine–2,4,6-triamine (melamine) molecules are assigned based on B3LYP/6-31G(d) quantum chemical calculations. Theoretical IR spectrum of melamine–3PTCDI complex is discussed in relation with the component molecules of the complex. Hydrogen bonding parameters and interaction energies for melamine–PTCDI complexes with one, two or three PTCDI molecules, as well as dimers formed from melamine and PTCDI molecules are calculated and different possibilities of auto-assembling observed by different groups are discussed in the light of present theoretical results. The energies and shapes of the frontier molecular orbitals and HOMO–LUMO gaps are calculated for neutral and ionic forms of PTCDI, for melamine and melamine–PTCDI complexes and compared to experimental data, where available.

STM/STS investigation of silicon adatoms (OPTOELECTRONICS AND ADVANCED MATERIALS - RAPID COMMUNICATIONS, IF 0.441)

[2009]

R. STIUFIUC*, B. GRANDIDIER, G. STIUFIUC

Linewidth of resonances in scanning tunneling spectroscopy (PHYSICAL REVIEW B, IF 3.908)

[2008]

L. Jdira, K. Overgaag, R. Stiufiuc, B. Grandidier, C. Delerue, S. Speller, and D. Vanmaekelbergh

Probing the Carrier Capture Rate of a Single Quantum Level (Science, IF 63.71)

[2008]

M. Berthe, R. Stiufiuc, B. Grandidier, D. Deresmes, C. Delerue, and D. Stievenard

Transport limitations and Schottky barrier height in titanium silicide nanowires grown on the Si(111) surface (Applied Physics Letters, IF 3.971)

[2007]

T. Soubiron, R. Stiufiuc, L. Patout, D. Deresmes, B. Grandidiera, and D. Stiévenard

Electronic and structural properties, of titanium silicide nanostructures formed on Si (111) 7x7 reconstructed surface (Journal of Optoelectronics and Advanced Materials, IF 0.587)

[2007]

R. Stiufiuc , T. Soubiron , B. Grandidier , D. Deresmes

Anisotropy and vortex behaviour in BiSrCaCuO thin films and multilayers probed by columnar pinning centers (The journal physica status solidi (a) - applications and materials science, IF 2.170)

[2006]

H Raffy, CD Murrills, A Pomar, G Stiufiuc, R Stiufiuc, ZZ Li

ANOMALOUS NORMAL STATE PROPERTIES OF UNDERDOPED Bi 2212 THIN FILMS (International Journal of Modern Physics B, IF 1.219)

[2006]

G Stiufiuc, R Stiufiuc, E Macocian, H Raffy, G Ilonca

SELF-DOPING EFFECT OBSERVED ON HEAVY ION IRRADIATED Bi 2212 THIN FILMS (International Journal of Modern Physics B, IF 1.219)

[2004]

R Stiufiuc, G Stiufiuc, E Macocian, H Raffy, G Ilonca

SYNTHESIS, MAGNETIC AND TRANSPORT PROPERTIES OF Ru1-xSbxSr2GdCu2O8 COMPOUNDS (International Journal of Modern Physics B, IF 1.219)

[2004]

G Ilonca, S Patapis, E Macocian, F Beiusan, T Jurcut, G Stiufiuc, R Stiufiuc

Superconductivity of MgB2 wires (Physica C: Superconductivity, IF 0.372)

[2003]

TR Yang, G Ilonca, AV Pop, R Stiufiuc, O Furdui

Critical currents of Bi:2212 doped by Fe and Ni (Physica C: Superconductivity, IF 0.372)

[2003]

G Ilonca, TR Yang, AV Pop, G Stiufiuc, R Stiufiuc, C Lung

GALVANOMAGNETIC EFFECTS AND ELECTRONIC SPECIFIC HEAT OF BULK La2-xBaxCu1-yZnyO4+d (International Journal of Modern Physics B, IF 1.219)

[2002]

G. ILONCA, A. V. POP, M. ILONCA, E. MACOCIAN, T. JURCUT, R. STIUFIUC and V. TOMA

Transport properties and ac susceptibility of (Bi1.6Pb0.4)Sr2Ca2Cu1−xCox)3Oy superconductors (International Journal of Inorganic Materials, IF 0.901)

[2001]

G Ilonca, AV Pop, Tzuen-Rong Yang, T Jurcut, C Lung, G Stiufiuc, R Stiufiuc, IA Panfilescu

Effects of rare earth ion substitution for Ca in (Bi, Pb): 2223 superconductors (International Journal of Inorganic Materials, IF 0.901)

[2001]

G Ilonca, AV Pop, Tzuen-Rong Yang, I Gr Deac, C Lung, R Stiufiuc, G Stiufiuc

TRANSPORT PHENOMENA IN THE MIXED STATE OF (Bi1.6Pb0.4) Sr2Ca2 (Cu1-xGax)3Oy BULK MATERIALS (Modern Physics Letters B, IF 1.668)

[2001]

G Ilonca, AV Pop, G Stiufiuc, R Stiufiuc, C Lung

ACTIVATION ENERGY OF Bi2Sr2Ca(Cu1-xFex)2O8+d THIN FILMS (Modern Physics Letters B, IF 1.668)

[2001]

G Ilonca, AV Pop, G Stiufiuc, C Lung, R Stiufiuc

MAGNETIC FIELD AND TEMPERATURE DEPENDENCE OF THERMALLY ACTIVATED DISSIPATION IN EPITAXIAL THIN FILMS OF YBa2 (Cu1-xZnx)3O7-d (Modern Physics Letters B, IF 1.668)

[2001]

Gh Ilonca, AV Pop, T Jurcut, E Mococean, C Beiuseanu, R Stiufiuc et al

TRANSPORT PHENOMENA IN THE MIXED STATE AND FLUCTUATION REGIME IN (Bi 1.6 Pb 0.4) Sr 2 Ca 1-x Ho x (Cu 1-y Zn y) 2 O 8+ d (Modern Physics Letters B, IF 1.668)

[2001]

G Ilonca, AV Pop, R Stiufiuc, G Stiufiuc, C Lung, S Patapis

TRANSPORT PHENOMENA IN La2-xBaxCuOy EPITAXIAL THIN FILMS (Modern Physics Letters B, IF 1.668)

[2000]

Gh Ilonca, AV Pop, T Jurcut, C Lung, G Stiufiuc, R Stiufiuc et al.

Structural properties of (Bi, Pb){sub 2}(SrBa){sub 2}(Ca {sub 1x} RE {sub x}) Cu {sub 3} O {sub y} bulk superconductors (Bulgarian Journal of Physics)

[2000]

G Ilonca, A Pop, C Lung, R Stiufiuc, G Stiufiuc, I Matei

Structural properties of (Bi, Pb) 2 (SrBa) 2 (Ca 1x RE x) Cu 3 O y bulk superconductors (Bulgarian Journal of Physics)

[2000]

G Ilonca, A Pop, C Lung, R Stiufiuc, G Stiufiuc, I Matei

CONFERENCES AND SEMINARS

Conferences

1. 16th International Conference on Nanostructured Materials, Sevilla, Spain, 6 – 10 June 2022, **Oral presentation**
2. 13th International Conference on Physics of Advanced Materials ICPAM-13, Sant Feliu de Guixols, Spain, 24 – 30 September 2021, **Invited Talk**
3. 6th European Conference on Cyclodextrins, Santiago de Compostella, Spain, 2-4 October 2019, **Oral presentation**
4. 257th American Chemical Society National Fall Meeting & Exposition, San Diego, CA, USA, 25-29 August 2019, **Oral presentation**
5. 6th Nano Today Conference, Lisbon, Portugal, 16-20 June 2019
6. 12th International Conference on Physics of Advanced Materials ICPAM-12, Heraklion, Crete, 22 – 28 September 2019, **Invited Talk**
7. XIV International Conference on Nanostructured Materials Nano 2018, Hong Kong, PRC, 24 – 29 June 2018, **Oral presentation**
8. 256th American Chemical Society National Fall Meeting & Exposition, Boston, MA, USA, 19 – 23 August 2018, **Oral presentation**
9. 9th International Conference on Advanced Vibrational Spectroscopy - ICAVS9, Victoria, BC, Canada, 11-16 June 2017
10. 11th International Conference on the Scientific and Clinical Applications of Magnetic Carriers, Vancouver, Canada, 31 May - 4 June 2016
11. Nanophotonics and Micro/Nano Optics International Conference, Paris, France, 7-9 December 2016, **Oral presentation**
12. 252nd American Chemical Society National Meeting & Exposition, Philadelphia, PA, USA, 21 – 25 August 2016, **Oral presentation**
13. 11th International Conference on Physics of Advanced Materials, Cluj-Napoca, Romania, 8-14 September 2016, **Oral presentation**
14. The Physics of Soft and Biological Matter, Cambridge, UK, 2016;
15. MRS Fall Meeting & Exhibit, Boston, USA, 29 November - 4 December 2015, **Oral presentation**
16. National Conference of Biophysics, Timișoara 2015, **Oral presentation**
17. Challenges in Nanoscience (ISAC2015), San Diego, USA, 17-20 August 2014;
18. International Conference on Nanoscience + Tehnology (ICN+T), Paris, Franța, 23-27 July 2012;
19. 8th NanoBioEurope 2012, Varese, Italia, 18-20 June 2012;
20. 10th International Symposium on Scanning Probe Microscopy & Optical Tweezers in Life Science, Berlin, Germania, 5-6 October 2011;
21. Process in Isotopes Molecules, 2011, Cluj-Napoca, Romania
22. 30th European Congress on Molecular Spectroscopy EUCMOS, Florența, Italia, 29 August – 3 September, 2010;
23. 11th Annual Conference" YUCOMAT 2009", Herceg-Novi, Muntenegru, August 31-4 September 2009;
24. 53rd International Symposium of the American Vacuum Society, San Francisco, SUA, 31 August – 4 September 2006;
25. European Conference on Surface Science ECOSS 24, Paris, Franța, 4-8 September 2006.

HONOURS AND AWARDS

Awards

Romanian Academy

Romanian Academy Award/"Constantin Miculescu" Prize for Physical Sciences (2018)

"Multifunctional nanostructures with applications in Nanomedicine"

INTERNATIONAL EXPERIENCE

Invited Professor

[26/11/2022 - 01/12/2022]

Invited Professor, University of ICELAND, Reykjavik, Iceland

Invited Researcher

[20/10/2019 - 25/10/2019]

Techniche Universitat Chemnitz, Germany

Invited Professor

[14/05/2016 - 21/05/2016]

Institute d'Electronique, Microelectronique et Nanotehnologie, Villeneuve d'Ascq, France

ORGANISATIONAL SKILLS

Organisational skills

coordinator as Principal Investigator (PI) of more than 7 interdisciplinary research grants in the field of Nanomedicine with a total value > 4.000.000 Euros

COMMUNICATION AND INTERPERSONAL SKILLS

Communication and interpersonal skills

good communication skills gained as a result of my teaching activities

JOB-RELATED SKILLS

Job-related skills

- good aptitudes for writing EU-funded grants as a consequence of my attendance at 17th International EU Grant Academy for Research and Innovation, 20-25 September, Portoroz, Slovenia
- national research grants evaluator (UEFISCDI)

BOOKS

Books

Co-author of the book entitled "Magnetic Nanoparticles in Nanomedicine", John Wiley & Sons, 2021

Author of the book entitled "Proprietăți electrice și de pinning ale supraconductorilor din clasa Bi:2212 dopați cu ioni ai metalelor de tranziție și conținând nanodefecte artificiale", Editura Risoprint, Cluj-Napoca, 2017

Co-author of the book entitled "Metode moderne de investigare a unor nanoobiecte cu aplicatii biomedicale", Editura Risoprint, Cluj-Napoca, 2013

NATIONAL AND INTERNATIONAL GRANTS PRINCIPAL INVESTIGATOR/RESPONSIBLE

National and International Grants Principal Investigator/Responsible

1. NATIONAL GRANT

Principal Investigator (PI)

Contract 68/2010 cod: PN II-RU-TE-2010-0259

Title: "Studiul interacțiunilor nanoobiectelor cu mediile celulare tumorale si posibilele lor aplicatii în terapia cancerului"

Period : 2010-2013

Project value : 750.000 RON;

2. NATIONAL GRANT

Principal Investigator/Responsible UMF (PI)

Contract 76/2012 cod: PN II-PT-PCCA-2011-3.1-1551

Title: "Profilaxia nanomediată a cancerului de colon la șoareci utilizând un vaccin sinergic nanoparticule conjugate cu MUC-1/Celule dendrice" - VACCINAN

Period : 2012-2016

Project value : 1.987.000 RON;

3. NATIONAL GRANT

Project member

Contract 125/2014 cod PN II-PT-PCCA-2013-4-1153

Title: "Tratamentul multimodal al cancerului pancreatic prin rezonanță plasmonică activată fototermic și chimioterapie selectivă mediată de biocompozite din argint" - NANOCHIM

Period : 2014-2016

Project value : 1.437.500 RON;

4. NATIONAL PROJECT

Project member

Contract 47/2013 cod PN II-ID-PCE-2012-4-0531

Title: "O nouă clasă de nanoparticule magnetice având potențiale aplicații în terapia cancerului"

Period : 2013-2016

Project value : 1.430.600 RON;

5. NATIONAL GRANT

Principal Investigator/Responsible UMF (PI)

Contract: 340/2015 cod PN II-RU-TE-2014-4-1770

Title: "Noi sisteme de transport a medicamentelor bazate pe PEGylați

multifuncționali"

Period : 2015-2017

Project value : 550.000 RON;

6. EUROPEAN FUNDS

Principal Investigator/Executive Director (PI)

Contract : 38/02.09.2016 ID 37_765, cod MySMIS: 103774

Title: "Dezvoltarea unei platforme de nanoscreening bazată pe SERS-TFF pentru detecția timpurie și evaluarea progresiei bolii în cazul cancerului de sân folosind probe de sânge - SEReNADE"

Period : 2016-2020

Project value: 9.162.169 RON;

7. INTERNAL GRANT UMF Cluj-Napoca

Mentor

Contract POSDRU/159/1.5/S/136893, finanțat prin Fondul Social European, Programul Operațional Dezvoltarea Resurselor Umane 2007-2013

Title: "Nanoparticule magneto-plasmonice cu aplicații în terapia cancerului"

Period: 2014-2015;

8. NATIONAL GRANT

Principal Investigator (PI)

Contract PN-II-ID-PCE-2011-3-0954, nr. 325/2011

Title: "Nanovezicule pentru transferul controlat al medicamentelor în celulele canceroase"

Period: 2011-2016

Project value: 1.499.740 RON.

9. NATIONAL GRANT

Principal Investigator (PI)

Contract 562/2009 cod IDEI 2606

Title: "Studiul interacțiunilor intermoleculare la scară nanometrică prin utilizarea tehnicilor de spectroscopie de forță atomică și nanolitografiere moleculară"

Period : 2009-2011

Project value : 990.120 RON

10. NATIONAL GRANT

Principal Investigator/Responsible UMF (PI)

Contract PN-III-P4-ID-PCCF-2016-0112

Title: "Nanomateriale magnetoplasmonice multifunctionale pentru aplicatii de tip point of care"

Period : 2018-2022

Project value : 8.500.020 RON