## Where today's life meets chemistry



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Rome, 5-8 September 2018



15<sup>th</sup> Eurasia Conference on Chemical Sciences

# Eurasia Conference on Chemical Sciences

Rome, 5-8 September 2018



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## Invitation



Dear Colleagues,

On behalf of the IOC, IAB, national and local Organizing, we would like to welcome you in Rome and we invite you to participate to the next Eurasia Conference on Chemical Sciences (EuAsC<sub>2</sub>S-15) that will be held at the Faculty of Civil and Industrial Engineering Sapienza University of Rome 5-8, September 2018. We hope you will contribute to a successful conference, fruitful for all participants. You can register online (starting from the beginning of February) on the web site of the conference (www.eurasia2018.org), as well as submit your contribution(s), for oral or poster presentation at the session of your choice.

The Universities of Sapienza, Rome, Italy, and of Salento, Lecce, Italy are organizing the Eurasia-15 Conference on Chemical Sciences. This is the 15<sup>th</sup> Eurasia conference and it will cover all

branches of modern chemistry.

All previous conferences in this series were organized in Asian countries, and only one in Europe, the 12<sup>th</sup> Eurasia, in Corfu' Greece; thus this will be the second conference of the series to be organised in Europe. The location of the conference is Rome, that is easily accessible by all countries, in the beautiful Renaissance Cloister of San Pietro in Vincoli near the Colosseo. The conference is expected to last 4 days and will take place between September 5<sup>th</sup> and 8<sup>th</sup>,2018.

More details about the scope, topics, travelling, accommodation, registration deadlines and fees can be found at the conference website, at **eurasia2018.org**. We look forward to see you in Rome at the beginning of September 2018.

After the successful experience of this international series, this conference will bring together leading chemists and young scientist to exchange scientific chemical information. The program includes Plenary and Invited lectures, session lectures and posters.

The main topics of the conference are the following:

- Inorganic Chemistry
- Organic, Biological and Medicinal Chemistry
- Agrochemistry and Food Chemistry
- Environmental and Green Chemistry
- Pharmaceutical Chemistry and Technology, Medicinal Chemistry, Natural Products in Medicinal Chemistry
- Physical Chemistry, Photochemistry, Electrochemistry, Spectroscopy, Thermochemistry
- Theoretical and Combinatorial Chemistry
- Analytical Chemistry
- Chemical Engineering
- Chemistry for Nanomaterials and Nanostructured Materials: Synthesis, Modeling, Characterization and Applications
- Chemistry of biomaterials
- Women in chemistry
- Chemistry and Ethics

#### Prof. Luciana Dini

Chair, National Organizing Committee

## Historical Background and Aim of Eurasia Conference

Around 1985-86, Prof. Bernd M. Rode from the University of Innsbruck, Austria suggested with Prof. Hitoshi Ohtaki (an International Steering Committee Member of the International Conference on Solution Chemistry (ICSC)) to organize an international conference concerning solution chemistry in Thailand. However, ICSC was scheduled until 1991, and thus, it was not possible to organize the new conference in Thailand before that year. Upon invitation of Profs. Rode and Ohtaki to Prof. Ivano Bertini of Florence University, Italy, to join this first committee, the three founders discussed the matter and changed Prof. Rode's original idea, to the creation of an international conference called Eurasia Conference on Chemistry of Solutions (EuAsC<sub>2</sub>S) with the aim to deepening friendship among chemists in the Eurasian supercontinent, and supporting them with the help of chemists in other continents such as America, Canada, and Australia This could be achieved with the organization of the international Eurasia series of conferences of world-top quality and class, mainly in developing Asian countries with the participation of a world-wide friendship network. Through this conference world-leading scientists were invited, with whom scientists, especially young ones from developing countries, could exchange scientific chemical information to emphasize scientific activities in their countries. Under such a vision of the three founders, Profs. Rode, Ohtaki and Bertini, the First Eurasia Conference on of Solutions (1<sup>st</sup> EuAs C2S) 1988 Chemistry was held in Bangkok in (http://xray.kaist.ac.kr/euasc2s/).

Eurasia Conference on Chemistry of Solutions changed its name to Eurasia Conference of Chemistry in Seoul in 1990, and then, again to Eurasia Conference on Chemical Sciences in 1992 in Guangzou due to its expansion to all areas of chemistry, now involved in the conference. All previous conferences in this series were organized in Asiatic countries; the first to be organized in Europe is the 12<sup>th</sup> in Greece. Chairman of Eurasia-12 is Emeritus Professor of Chemistry Nick Hadjiliadis. The logo of the conference is *EuAsC<sub>2</sub>S*, which was proposed by Dr. Sunt Techakumpuch of Chulalongkorn University, Thailand, in 1988. The Eurasia Conferences on Chemical Sciences Chairman is a member of the International Organizing Committee (IOC) at each conference and has a general supervision of the organization and the Chairman of the National Organizing Committee (NOC), is the one responsible to organize the conference with the cooperation of the National (Local) Organizing Committee. Besides these committees, EuAsC<sub>2</sub>S has also the International Advisory Committee (Board) in which world-leading scientists are contributing to support the activities of the conference. At present, EuAsC<sub>2</sub>S has 37 members from 28 countries.

## **International Organizing Committee (IOC)**

Atta-ur-Rahman, Pakistan Bruno Botta, Italy Iqbal M. Choudhary, Pakistan Srinivasan Chandrasekaran, India Nick Hadjiliadis, Greece Susumu Kitagawa, Japan Musa Z. Nazer, Jordan Bernd Michael Rode, Austria Hyunjoon Song, Secretary, Korea

### **EuAsC<sub>2</sub>S FOUNDER**

Ivano Bertini, Italy (passed away, 2014) Hitoshi Ohtaki, Japan (passed away, 2006) Bernd Michael Rode, Austria

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## **International Advisory Board (IAB)**

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## National Advisory Board (NAB)

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ASSOCIAZIONE ITALIANA PER LA RICERCA INDUSTRIALE

## Local Organizing Committee (LOC)

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## **Staff Members**

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Elisa Panzarini	

## Staff and Administration Supervisor: Cristina Gippa



## Sapienza University of Rome

With over 700 years of history, 111,000 students, 4000 teachers and 2000 employees, technicians and librarians, in addition to 2000 administrative staff in university hospitals, Sapienza is the first university in Europe. Our mission is to contribute to the development of a knowledge society through research, excellence, quality education and international cooperation.

#### POSITION ON THE INTERNATIONAL PANORAMA

The world's leading university rankings place Sapienza at the forefront among Italian universities, for quality of research and teaching and for its international dimension. In the sectoral charts, the University excels and qualifies as a benchmark for many disciplines.

#### **EDUCATION AND SERVICES FOR STUDENTS**

Sapienza currently offers over 250 programmes and over 200 vocational master courses. The School of Advanced Studies provides a programme of excellence and free tuition for the best students. Students with a high school score of 100 are exempt from enrolment fees, and the bonus is extended if they keep up their good grades. Families who have more than one child enrolled at the university also enjoy a special brothers-sisters bonus.

University services include 55 libraries (two with 24H reading rooms), 18 museums, Ciao and Hello orientation desks, a Sort – Orientation and Tutoring Office in each faculty, a Disabled Students Office, the Job Soul Placement Office, and a Public Relations Office. Sapienza University promotes a vast range of cultural, social and sports activities and has various facilities (over 100,000 square meters) for sports, music, theatre and a web

radio.

Over 30,000 students come from other Italian cities, nearly 8000 are foreign and over 3300 students a year come to Sapienza as part of international mobility programmes.

Thanks to a wide network of collaborations with universities around the world, Sapienza also provides its students many international opportunities, including double degrees, scholarships abroad, internships in different European and non-European countries, international doctorates.

#### RESEARCH

Scientific research activity at Sapienza covers an extremely broad spectrum of disciplines, reaching levels of excellence in many areas, including archaeology, physics and astrophysics, humanities and cultural heritage, the environment, nanotechnologies, cell and gene therapy, design, aerospace, social and economic sciences.

Nobel Prize winners and internationally renowned scientists have taught or studied at Sapienza.

#### **STRUCTURES**

Sapienza is organized into 11 faculties and 63 departments, as well as numerous research and service centres. Management operates in a central administration organized by areas, offices and sectors.

The rectorate is collegiate; beside the Rector, there is a Deputy Rector and a group of Assistant Deputy Rectors and delegates with specific competences, alongside committees and commissions for evaluation, strategic planning, quality and integration of activities.

## **Conference Plan**

	AM3 12.30-13.00	it of Eurosia 16 Amony with	ra) priisol) ramaanuonnA	
Saturday 3 September	AM2 11.00-12.30	Chemical-physical approaches for detection and characterization X.A	Material chemistry & technology X.B	
~	1MA 05.01-00.00	C-based materials <i>IX.A</i>	Chemical technologies for life science II <i>N.B</i>	
	PM3 17.30-19:00	รชินุวออน g	AI bno 201	
	PM2 16.00-17.30	Proteomics and metabolomics II V/III.A	Agrifoad VM.B	
Friday September	PM1 14.00-15.30	Proteomics and metabolomics 1 V/II.A	Biomaterials - nanomedicine VIII.B	
7.	AM2 11.00-12.30	Pharmaceutical chemistry II VI.A	Chemistry for nanomaterials VLB	SESSION
	0E.01-00.20	Pharmaceutical chemistry I V.A	Chemical technologies for life science I VB	POSTER
	PM2 16.00-17.30	Catalysis IV.A	Innovative materials for biomedical applications N.B	
day mber	PMI 14.00-15.30	Inorganic chemistry III.A	Theoretical chemistry III.B	
Thursd 6 Septer	AM2 11.00-12.30	Supramolecular chemistry ILA	Computational chemistry ###	
	AMI 09.00-10.30	Analytical chemistry IA	Physical chemistry for nanomaterials I.B	
esday ember	PM2 16.00-17.30	səəntəəy	Albuaj <u>a</u>	
Wedne 5 Sept	PMI 14.00-15.30	sə <i>n</i> ıtəə7 ləqoV	l bno gninsqO	

## **List of Nobel and Plenary Lecturers**

**Jean-Marie Lehn**, Nobel Laureate, Université de Strasbourg (Strasbourg, France) *Perspectives in Chemistry: Towards Adaptive Chemistry* 

Muhammad Iqbal Choudhary, International Center for Chemical and BiologicalSciences, University of Karachi (Karachi, Pakistan)Efficient Approaches for Drug Discovery and Development

**Alberto Diaspro**, Istituto Italiano di Tecnologia (Genova, Italy) *Multi-Messenger Optical Nanoscopy Merging Biology, Chemistry and Physics* 

### Nobel Lecturer- Professor Jean-Marie Lehn, Nobel Laureate



Jean-Marie LEHN was born in Rosheim, France in 1939. In 1970 he became Professor of Chemistry at the Université Louis Pasteur in Strasbourg and from 1979 to 2010 he was Professor at the Collège de France in Paris. He is presently Professor at the University of Strasbourg Institute for Advanced Study (USIAS). He shared the Nobel Prize in Chemistry in 1987 for his studies on the chemical basis of "molecular recognition" (*i.e.* the way in which a receptor molecule recognizes and selectively binds a substrate), which also plays a fundamental role in biological processes.

Over the years his work led him to the definition of a new field of

chemistry, which he has proposed calling "supramolecular chemistry" as it deals with the complex entities formed by the association of two or more chemical species held together by non-covalent intermolecular forces, whereas molecular chemistry concerns the entities constructed from atoms linked by covalent bonds. Subsequently, the area developed into the chemistry of "self-organization" processes and more recently towards "adaptive chemistry", dynamic networks and complex systems.

Author of more than 1000 scientific publications, Lehn is a member of many academies and institutions. He has received numerous international honours and awards.

Jean-Marie Lehn is Professor at the University of Strasbourg Institute for Advanced Study (USIAS), Honorary Professor at the Collège de France in Paris and Emeritus Professor at the University of Strasbourg. In 1968, he achieved the synthesis of cage-like molecules (cryptands) containing a cavity (crypt) into which another entity, molecule or ion of specific nature, can be lodged, forming a cryptate. This work expanded into the investigation of the chemical basis of "molecular recognition" (the way in which a receptor molecule recognizes and selectively binds a substrate), which plays a fundamental role in biological processes. Over the years these studies led to the definition of a new field of chemistry, which he called "supramolecular chemistry". It deals with the complex entities formed by the association of two or more chemical species held together by intermolecular forces.

In 1987, Jean Marie Lehn was awarded the **Nobel Prize in Chemistry**, together with Donald Cram and Charles J. Pedersen.

### Plenary Lecturer n. 1 - Professor Muhammad Iqbal Choudhary



Born in 1959, in Karachi, Pakistan, he is a professor at the HEJ Research Institute of Chemistry, University of Karachi, Pakistan. Prof. Choudhary earned his PhD from the HEJ Institute – in Organic Chemistry in 1987, and his M. Sc. degree in 1983 from the University of Karachi, Pakistan, also in Organic Chemistry. He also did his B. Sc. degree at the University of Karachi in Chemistry, Biochemistry, and Botany.

Prof. Choudhary has 1016 publications (Citations 13,000, h index 44) in the fields of organic and bioorganic chemistry, along with 60 international patents (46 US Patents), 59 books and 40

chapters in books, published by major U.S. and European presses. On the basis of his researches, 73 students have been awarded PhD degrees in various areas of natural product and bioorganic chemistry.

Since 1990, he has been among the world leaders in the field of natural product chemistry, and has made pioneering contributions in the discovery of novel natural products. He has discovered many potent anti-epileptic and anti-leishmanial compounds from indigenous medicinal plants that are under clinical trials. His contributions to reverse bacterial resistance to antibiotics represent seminal contributions in this important field. He leads one of the developing world's finest research centers of natural product chemistry (HEJ Research Institute of Chemistry) since 2002, and has trained many of young researchers, especially women, from across the Afro-Asian region in natural product chemistry. He has established several research centers in Pakistan, and helped to setup research units in Africa, and South and Central Asia. His scientific, and capacity building contributions have been recognized by prestigious national and international awards and honors, and fellowships of several academies of science.

He is a Fellow of the Islamic World Academy of Sciences (IAS) and is involved in nationally important projects of academic nature including; the survey of medicinal plants in Pakistan, environmental monitoring, capacity building in science and technology in Pakistan, etc. He is also involved in industrial projects and currently heading the largest "Industrial Analytical Centre" of Pakistan. He is also currently the project director of the newly established "Dr Panjwani Centre for Molecular Medicines and Drug Development."

### Plenary Lecturer n. 2 - Professor Alberto Diaspro



Alberto Diaspro is Director of the Department of Nanophysics at the Istituto Italiano di Tecnologia (IIT), Deputy Director of IIT, Chair of the Nikon IMaging Center at IIT (www.nic.iit.it). AD is Professor of Applied Physics at the Department of Physics of University of Genova and supervisor for the Ph.D. Courses in the Bioengineering and Robostics and Physics programs of the Universitry of Genova within the IIT program. He was President of OWLS (Optics with Life Sciences), EBSA (European Biophysical Societies Association) and Appointed Vice President of ICO (Interational Commission of Optics). AD is afounder of the Nanoscale **Biophysics** Subgroup of the Biophysical

Society. During the 90's he carried out part of his research activity at Drexel University (PA, USA), Universidad Autonoma de Madrid (Spain) and Czech Academy of Sciences (Czech Republic). He also coordinated a research program (2004-2012) at IFOM-IEO Campus in Milano on Biomedical Research and is currently associated with the Institute of Biophysics of the National Research Council (CNR)(since 2006). He founded LAMBS (Laboratory for Advanced Microscopy, Bioimaging and Spectroscopy) in 2003 - www.lambs.it. AD realized a hybrid artificial "nanobiorobot" within EU and national Research Projects (2000-2005), and designed and realized the first Italian multiphoton microscope within a research grant of the National Institute of Physics of Matter (1999). He directed the design and realization of the first Italian nanoscopy architecture at the Neuroscience and Brain Technologies Department of IIT (2008).

At present, Alberto Diaspro coordinates the Nanobiophotonics IIT research program. He is coordinator of several EU and national research programs, and published more than 300 international peer reviewed papers, 6000 citations, H=38 (source Google Scholar). He is Editor in chief of the international journal Microscopy Research and Technique and active member of international editorial boards and societies (SIOF, SIF, SISM, SIBPA, BS, EBSA, OWLS, IEEE, SPIE, OSA).

AD is IEEE senior member and SPIE fellow (http://spie.org/profile/Alberto.Diaspro-6137).

His specific research experience is related to the design, realization and utilization of optical and biophysical instrumentation as far-field super resolution optical microscopy and nanoscopy, conventional and confocal microscopy, two-photon fluorescence microscopy and spectroscopy architecture, differential scanning calorimetry, scanning probe microscopy (STM, SNOM, AFM), polarized light scattering, signal and image digital processing. His main interests are molecular oncology (chromatin, endocytosis and adhesion mechanisms), neuroscience (brain mapping and neuronal network signalling) and smart materials (intelligent drug delivery and nanocomposite materials).

# September 5<sup>th</sup> Nobel and Plenary Lectures

Chair: Bernd Michael Rode Honorary President of ASEA-UNINET and EuAsC<sub>2</sub>S Founder, Austria

#### NL

## Perspectives in Chemistry: Towards Adaptive Chemistry

#### <u>Lehn J.M.</u>

### ISIS, Université de Strasbourg, France lehn@unistra.fr

Supramolecular chemistry is intrinsically a dynamic chemistry in view of the lability of the interactions connecting the molecular components of a supramolecular entity and the resulting ability of supramolecular species to exchange their components. Similarly, molecular chemistry becomes a dynamic covalent chemistry (DCC) on introduction into the molecular entity of covalent bonds that may form and break reversibly, so as to allow a continuous change in constitution by reorganization and exchange of building blocks. Taken together, these features define a Constitutional Dynamic Chemistry (CDC) covering both the molecular and supramolecular levels.

CDC introduces a paradigm shift with respect to constitutionally static chemistry. It takes advantage of dynamic diversity to allow variation and selection and operates on dynamic constitutional diversity in response to either internal or external factors to achieve adaptation.

CDC generates networks of dynamically interconverting constituents, constitutional dynamic networks, presenting agonistic and antagonistic relationships between their constituents that may respond to perturbations by physical stimuli or to chemical effectors. It applies in chemistry as well as in materials science.

The implementation of these concepts points to the emergence of adaptive and evolutive chemistry, towards systems of increasing complexity.

#### References

J.-M. Lehn, Supramolecular Chemistry: Concepts and Perspectives, VCH Weinheim Ed. 1995.

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J.-M. Lehn, Angew. Chem. Int. Ed. 2015, 54, 3276.

#### PL-1

### Efficient Approaches for Drug Discovery and Development

Choudhary M.I., Rahman A.

International Center for Chemical and Biological Sciences, H. E. J. Research Institute of Chemistry and Dr. Panjwani Center for Molecular Medicine and Drug Research, University of Karachi, Karachi-75270, Pakistan

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As developing world face food security issues, it also confronts with the drug insecurity challenges. Nation states must prioritize the agenda for developing safe and effective drugs against local diseases. The current drug development paradigm is cost, time and labor intensive, which developing countries cannot afford to invest. There is, therefore, a need of appropriate, efficient and cost-effective strategies for drug development, which must be based on indigenous knowledge resource base, S&T capacity, and people-friendly approval process. In last two decades, we identified a large number of new and novel chemical substances, and their synthetic analogues with potent activities against various disease- related targets.

Multidrug resistance is a challenging problem for the health care sector and is very common in familiar pathogens, such as vancomycin-resistant Enterococci and Staphylococcus aureus. Exposure and inappropriate use of the antibiotics is the major cause of MDR, both in developed and developing regions. Our study, focusing on the discovery of natural and synthetic compounds, active against multidrug resistant bacteria Staphylococcus aureus and Pseudomonas aeruginosa have resulted in the identification of several novel and potent inhibitors of MDR Staphylococcus aureus (EMRSA-17, EMRSA-16, MRSA-252, and Pak clinical isolates) from natural sources. Resistance-reversal studies at molecular level were carried out by employing flow cytometric, microscopic, and spectroscopic techniques. Synergistic and partial synergistic effects of these compounds, in combination with antibiotics, were investigated. This work has so far resulted in the identification of several novel "helper molecules", which can increase the efficacy of existing antibiotics to over 1000-fold in some cases. Breast cancer is the most common cancer in women worldwide, with nearly 1.7 million new cases diagnosed in 2014 (second most common cancer overall). This represents about 12% of all new cancer cases and 25% of all cancers in women. Incidence rates vary from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe. In most of the developing regions the incidence rates are below 40 per 100,000. It has been reported in 2015 as the most prevalent cancer in women. Approximately one-third of all breast cancer patients and two-thirds of postmenopausal breast cancer patients have hormone-dependent (estrogen-dependent) breast cancers, which express estrogen receptors and require estrogen for tumor growth. Aromatase inhibitors are currently being tested as primary prevention therapy in large randomized trials. While only a few chemotherapies such as exemestane and tamoxifen are in clinical practices for the inhibition of aromatase functions. Therefore, there is a need to identify new structural analogues of available drugs and evaluate their

anticancer potential. In this study, we will synthesize the new derivatives of existing aromatase inhibiting drugs through biotransformation and conventional synthesis and evaluate their potential against aromatase enzyme. During this research we have synthesized a number of new structural analogues of aromatase inhibitors and other steroidal drugs including exemestane, formestane, testolactone, mibolerone, boldenone, indomethacin, levonorgestrel, through biotransformation. This has provided an efficient method for the synthesis of new analogues of existing aromatase inhibitors. The new analogues of the mentioned drugs were found to be moderate to potent inhibitors of aromatase enzyme as compared to standard drugs letrazole, and exemestane. Epilepsy is a group of chronic nervous system disorders, characterized by recurrent of seizures which are caused by inappropriate electrical firing of neurons in different parts of brains, leading to abnormal body movements. About 50 million people worldwide have epilepsy; with almost 90% of these people being in developing countries. Epilepsy is non curable disease, but can be controlled and managed with medications. Unfortunately most of anticonvulsant drugs available in the market are synthetic in nature, and associated with severe side effects and have to be used whole life to control the seizures. Through extensive studies on medicinal plants of family Ranunculaceae, anticonvulsant natural products, isoxylitones, were discovered from medicinal plants Delphinium denudatum, and also detected in non alkaloidal aqueous extracts of Aconitum cochleare, Aconitum laeve, and Delphinium nordhagenii. Delphinium denudatum was found to exhibit a good anticonvulsant activity in in vivo animal models of epilepsy. Bioassayguided isolation studies on the roots of this plant, afforded a non-toxic and nonalkaloidal aqueous extract, which exhibited strong anticonvulsant activities in in vivo animal models of epilepsy, such as MEST test, scPTZ, scBIC, scPTX, and scSTN tests. Further purification of aqueous extract led to isolation of a strongly anticonvulsant isomeric mixture of E/Z isoxylitones which were then synthesized to investigate their anticonvulsant activities in *in vitro* and *in vivo* tests of epilepsy. Studies have shown a potent anti-epileptogenic activity of isoxylitones in scPTZ-induced kindling model in mice and they also found to affect some of the underlining molecular changes that are induced following the seizures. Isoxylitones (E/Z) blocked the Na<sup>+</sup> current in a concentration dependent manner ( $IC_{50} = 184.9$  nM). These compounds were also subjected to various toxicological studies and compound did not exhibit LD<sub>50</sub> up to the dose of 1,000 mg/kg and were found to be harmless to the model animals with higher potency as antiepileptic compounds than the currently available drugs. During this presentation, underlying philosophy and approach of our research on cost-effective discovery of lead molecules by using ethnobotany, natural product chemistry, and drug repositioning strategies will be discussed.

#### PL-2

## Multi-Messenger Optical Nanoscopy Merging Biology, Chemistry and Physics

#### <u>Diaspro A.</u>

Nanoscopy, Istituto Italiano di Tecnologia, Genova, Italy Department of Physics, University of Genoa, Genova, Italy alberto.diaspro@iit.it

A Multi messenger microscope implemented within a liquid and tunable strategy is presented. Such an approach is liquid because it aims to overlap different mechanisms of contrast and it is tunable due to its tunability in terms of spatial and temporal resolution using single-molecule localization, STED and label-free solutions to contribute to answer questions in cellular and molecular biology like the ones related to the way chromatin structures in the nucleus are ruling the compaction and function of the human genome in the interphase of cells and mitotic chromosomes.

Nowadays, one cannot escape merging biology, chemistry and physics to address scientific and technological problems. Light microscopy offers a unique chance, starting from the "soft" light-matter interaction, to investigate matter recording different signals coming from light stimuli in the visible region, say, at low level of perturbation. A further demonstration of our assumption lies in the motivation of the Nobel Prize in Chemistry in 2014 for developments in super-resolved fluorescence microscopy. The modern optical microscope operates in the nanoscopy domain and is able to detect different messages coming from illuminated samples under the mechanisms of fluorescence parameters from lifetime to single molecule emissions, scattering associated to specific structural organization of the specimen and polarization to monitor specific configurations. Linear and non-linear interactions in the coherent and incoherent domains will be addressed including computational and modelling aspects. New approaches like image scanning microscopy in the optics domain and expansion microscopy in the chemical domain will be presented towards the study of biological systems.

Correlative optical and force nanoscopy [1] and liquid tunable microscopy [2] will be discussed.

#### References

[1] C. Smith, *Nature*2012, *492*, 293.
[2] R. Won, *Nature Photonics* 2018, *12*, 259.

## **Parallel Sessions**

## September 6<sup>th</sup>

# Session I.A Analytical Chemistry

Chair: Giovanni Natile University of Bari, Italy

#### I.A-1 - Key-Note Lecture

### Electronic Cigarettes: an Important Progress or Just Another Risk for Health?

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In the past decade, electronic cigarettes and the chemical substances used in them, the so-called E-liquids, have enormously developed in technology and variety, leading to a billion-dollar market. The main reason for this development is the hope that E-cigarettes are a suitable substitute for tobacco-smoking, diminishing the health risks associated with smoking without invoking the painful experiences associated with quitting it. The large variety of flavors provided by the E-liquid producers has facilitated the change from smoking to 'vaping' as the use of E-cigarettes is rightly called, as it is based on evaporisation at moderate temperatures instead of combustion at much higher temperature. Although studies available until now suggest that much less health risks are caused by vaping compared to smoking, the large variety of aromas used in the liquids and of devices available demand much more detailed and critical evaluation of potential risks. We have, therefore, decided to perform chemical and biological tests of the vapor inhaled, under standardized conditions with numerous liquids, in particular the most-selling ones on the market. The results obtained so far indicate that the assumed reduction of health risks is valid, but that certain vaping conditions and a number of aromas being used can induce new problems and potential risks. The performance of further studies of this kind seems extremely important, therefore, in order to confirm the advantages of vaping versus smoking, to avoid hazardous substances and to create science-based directives and hence legislation. At present, legislation strongly differs from country to country, ranging from almost complete banning to financial support for changing from tobacco to electronic cigarettes, and studies of the type presented here should provide a good basis for future decisions and regulations.

#### I.A-2

## Repeatability of FTIR in Quantitative Asbestos Analysis: Inter-instruments Test for Low Concentrations

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Infrared Spectroscopy (FTIR) is widely used as a technique for the analysis of asbestos containing materials. It is capable of detecting asbestos even in small quantities and in complex matrices. In this work, we present an operative protocol for the comparison of three FTIR instrumentations, for use quantitative analytical methods to detect low amount of chrysotile in bulk samples with complex matrix. To investigate and rank the repeatability of the analysis method, the coefficient of variation (CV) or relative standard deviation was used as a benchmark parameter. The smaller the CV is the smaller the scatter of results (in terms of standard deviation) relative to the mean value of a sample: thus, a small CV correlates with a high repeatability. One of the main tasks of this group was the constitution of a proficiency test to evaluate the capability of the equipment to obtain results with good reproducibility. The test became an effective tool to detect malfunctions and other deviations to its normal work. Calibration curves were built with 4 analytical points for each analytical band, by plotting the net area of the band integrated from the baseline to its minimum of absorption. The same set of bulk samples with low concentration of chrysotile were analyzed by three experienced laboratories equipped with three different instrumentations. The same single expert operator that used a validated internal protocol realized every set of five pellets. The two worst pellets, which showed inhomogeneities, lesions, opacities, or imperfections were rejected. Six IR spectrum acquisitions were performed for each of the remaining three pellets, three for each pellet side in order to mediate possible inhomogeneities invisible with naked eye. An average area and deviation standard of each studied IR band was obtained. The samples studied had a concentration of 2% in chrysotile. The three different instrumentations detected the set of samples with a CV lower than 10%. So we can considered the inter-instruments protocol with a low variance and a good repeatability to detect chrysotile.

#### I.A-3

## Further Developments in the Methodology of Quantitative Analysis by FT-IR: Quantitative Detection of Low Chrysotile Concentrations

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The standard methodologies for quantitative analysis of asbestos using Fourier transform infrared (FTIR) instruments have specially evolved in the preparation of the pellets. In this work, we present an operative validate protocol to detect low concentrations of chrysotile in bulk samples with complex matrix. This new protocol improves transparency and homogeneity of the pellets reducing inhomogeneities, lesions, opacities and/or others imperfections. Two distinct skilled laboratories have analyzed all the set of samples to investigate and rank the reproducibility of the analysis method. Calibration curves for every laboratory were built with four analytical points for each analytical band for low concentrations  $(0 - 500 \mu g)$ . The same set of bulk samples (2-6%) of chrysotile were separately prepared and analyzed by the two expert laboratories. The same single validated internal protocol was used to realize the pellets of calibration curves and every set of pellets of bulk sample. Six IR spectrum acquisitions performed for each of the better pellets. An average area and deviation standard of each studied IR band was obtained. The results of the two laboratories were compared for all set of the samples. The goodness of the analytical method have been evaluated using a statistical approach (t test). The protocol can be considered reproducibly for the statistical results. However, it is important to choose the analytical band to quantify chrysotile based on the matrix complexity of the samples. The chosen bands for quantitative analysis were between 3692 - 3630 cm<sup>-1</sup> and the band around 606 cm<sup>-1</sup>. It is preferable, if possible, to use peaks without interferences or present in the fingerprint region.

Analytical Chemistry

I.A-4

### Heavy Metals in Laguna Lake, Philippines: Spatial and Temporal Variations

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Many lakes around the world are a source of livelihood. With increasing population and changing land use, however, these lakes may become polluted with typical water contaminants such as nutrients, pesticides, industrial chemicals and heavy metals in addition to the rising number of emerging contaminants. Many water contaminants particularly the heavy metals are relatively stable in aqueous systems and are not totally removed in conventional wastewater treatment and post-discharge processes. Laguna Lake is the largest and one of the economically important lakes in the Philippines. It has many uses such as aquaculture, source water for industrial and agricultural purposes, water source for potable water production, transport and recreation, floodwater reservoir, and as a final sink for effluents from the domestic, industrial and agricultural activities around the lake. We studied the priority heavy metals Pb, As, Cr, Cd, and Hg along with the other metals (Ni, Co, Mn, Cu, Zn) in surface waters from nine sampling sites in the lake. The water samples were analysed using the standard analytical determination methods ICP-MS and AAS (cold vapor and hydride generation). The heavy metal concentrations are generally higher in the West part of the Lake than in the East part which indicates anthropogenic inputs from the urban sprawl and industries along the Western side of the lake. The concentrations vary also with time which may depend on the water conditions during wet and dry seasons. Geostatistical prediction maps using inverse distance weighted interpolation were created to show spatial distribution of the heavy metals in the lake. Recent lake-wide concentrations of the heavy metals and spatial patterns identified the Western part of the lake as the priority area for stringent environmental monitoring and management because of potential risks to human and ecological health.
# **Session I.B**

# **Physical Chemistry for Nanomaterials**

Chair:

*Karine Mougin Institut de Science des Matériaux de Mulhouse, France* 

## Poly Lactic Acid films with Dispersed Cellulose Nanoparticles: a Study on the Gas Transport Properties and Impurities Degasing Kinetics

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The gas transport properties and the impurity degassing kinetics of biopolymer nanocomposites made of a PolyLactic Acid (PLA) matrix with dispersed rod- shaped cellulose nanoparticles (CNC) were studied by gas phase permeation technique and Thermal Desorption Spectroscopy (TDS). Biopolymer nanocomposites with lauryl-chloride/chlorododecane (CH<sub>3</sub>(CH<sub>2</sub>)<sub>10</sub>CH<sub>2</sub>Cl) functionalized CnP with content up to 10 wt. % were prepared using PLA-CHCl<sub>3</sub> and CNC-CHCl<sub>3</sub> solutions. Films with thickness in the 50 m range were prepared casting the mixed solutions in a Petri dish until complete solvent evaporation. The characterization of the pure PLA matrix and of the nanocomposite samples was carried out by Scanning Electron Microscopy (SEM) to obtain information on the filler dispersion degree and by Differential Scanning Calorimetry (DSC) to obtain information of variation of the glass transition temperature and crystalline fraction with filler content while the mechanical properties were analyzed by Dynamic Mechanical Thermal analysis (DMTA).

Gas transport experiments were carried out using penetrant molecules with different molecular size and condensation properties ( $CO_2$ ,  $N_2$ ,  $D_2$  and He) in the 295 to 350 K temperature range. Results indicate the gas transport through the pure PLA matrix and the nanocomposite samples obeys the solution-diffusion mechanism and that no plasticization effects occur upon penetrant permeation. Experimental results reveal a clear correlation between the change of the structural and mechanical properties of nanocomposite samples, as function of the filler content, and the gas transport parameters, namely penetrant diffusion constant and permeability. The apparent values of the activation energy for diffusion and permeation don't change with filler addition suggesting that the filler particles act as diffusion obstacles in the penetrant migration paths through the PLA matrix layers.

TDS experiments carried out with a quadrupole mass spectrometer evidence that degassed impurities mostly consist of absorbed solvent. The impurity degassing kinetics was analyzed to obtain information on the rate limiting step as function of the filler content. Results are discussed in the framework of the free volume theory for diffusion considering the gas impermeable nature of the CNC additive as well as the CNC agglomeration process.

## Carbon Quantum Dots-Fullerene Hybrid Langmuir Schäfer Films for Photoinduced Phenomena

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Carbon quantum dots (CQDs) are recently derived and considered from carbon allotropes family, they were firstly discovered during the purification of singled walled carbon nanotubes (SWCNTs), having sizes less or equal to 10 nanometers [1]. CQDs have excellent optical properties, good biocompatibility, great aqueous stability, low cost, simple synthesis, etc. Many synthesis routes and methods utilizing different precursors could be followed and mainly classified as top-down and bottom-up approaches [2]. In this work, negatively charged nitrogen doped CQDs were synthesized by a fast pyrolysis method using ethanolamine as a precursor and hydrogen peroxide as oxidant agent [3]. The prepared CODs were characterized by means of different analysis techniques such as UV-Vis spectroscopy, FTIR spectroscopy, steady state fluorescence spectroscopy in addition to transmission electron microscope (TEM) and Z-potential measurements. CQDs were used as building block for the development of an innovative hybrid nanostructured thin solid film of CODs-double charged fullerene derivative (fulleropyrrolidines) **FP2** supramolecular adduct by means of electrostatic (ES) interactions. First of all, the CQDs fluorescence quenching in presence of increasing **FP2** concentration in aqueous solution was investigated by constructing a Sterm Volmer plot, confirming the possibility to exploit such a dyad for the design of electronic devices [4]. Then, FP2 was spread at air-water interface of a Langmuir trough containing CQDs as subphase, ES interactions occurred among FP2 positively charged derivatives and negative charges of CQDs, as demonstrated by z-potential analysis. The Langmuir isotherm showed a marked shift towards higher limiting area value confirming the CQDs-FP2 supramolecular adducts formation. The floating layer was transferred by the Langmuir-Schafer method (LS) onto quartz and ITO/glass slides for further analysis and also onto FTO/glass for conducting photoiduced phenomena. Uv-Vis absorption, photoluminescence (PL) spectra and FTIR analysis were carried out ensuring the successful transfer of the supramolucalr adduct, underlining the great potential of such an approach that allowed the immobilization of hydrosoluble CQDs on solid films that can be employed for several applications such as photocurrent generation or photodetection [1].

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## New Frontiers in Bio-Sustainable Multifunctional Materials: Ceramic Templated Eumelanin-like Nanostructures

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Organo-inorganic hybrids hold great promise for the design of new multifunctional materials with a large spectrum of known and as yet unknown properties. The need to address bio-sustainability issues has raised huge interest toward biocompatible and bioinspired materials boosting the investigation and the engineering of biomedical devices based on natural products. Among those, eumelanins, ubiquitous biological pigments, as well as eumelanin-like compounds, hold huge potential in developing biologically active materials, thanks to their intrinsic biocompatibility, biodegradability and multiple biological functions, including photoprotection, photosensitization, free radicals scavenging, metal ion chelation, protein binding and even intrinsic antimicrobial behavior. Furthermore, due to their semiconductor behavior and electrical properties they hold great promise for nextgeneration photovoltaics and bioelectronics. Eumelanins are produced in-vivo by oxidative polymerization of phenolic or indolic compounds within melanosomes that template melanin formation. We recently proved that eumelanins biological functions can be markedly enhanced if their formation occurs in the presence of a nanostructured ceramic phase, acting as catalyst and structure directing agent in biopolymers building up, thus mimicking melanosomes functions according to a bioinspired approach [1-4]. In this way, TiO<sub>2</sub> high photocatalytic activity was exploited to drive 5,6-dihydroxyindole-2-carboxylic acid (DHICA) polymerization to eumelanin, via complex mediated electron transfer (LMCTC) involving DHICA and Ti<sup>4+</sup> ions, that enabled TiO<sub>2</sub> photo-activation under visible light [1]. Obtained eumelanin-TiO<sub>2</sub> hybrid nanostructures showed striking antimicrobial activity even higher than bare melanin under visible light and peculiar antimicrobial mechanism [2,3]. This synthesis strategy was successfully extended to the design of stable, bioactive and biocompatible melanin-silica hybrid nanoparticles with potent antioxidant and cytoprotective activity associated with a specific subcellular localization [4]. Both systems disclose the great potential of this approach, that can be extended to eumelanin like compound in agri-food wastes, ultimately leading to cutting-edge functional hybrid materials featuring relevant biological properties, such as antimicrobial activity, selective cell interaction and signaling, as well as ionic- and electronic-based charge transport.

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## A Reinvestigation of the Deceptively Simple Reaction of Toluene with HO, and the Fate of the Benzyl Radical

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Toluene is one of the main anthropogenic aromatic molecules in the atmosphere, due to cars exhaust, solvent use and biomass burning. Its reactions with the hydroxyl radical contribute to ozone deple-tion and aerosol forming in the atmosphere.

There is a general consensus in that the most important reactions are addition to the benzene ring, leading to cresols, and H-abstraction from the methyl group, leading to the benzyl radical which can further react with  $O_2$ , eventually producing benzaldehyde. Several experimental and theoretical studies, however, differ about the structure of the products and their relative abundance. The present work, part of a larger systematic study on all the possible reaction mechanisms of toluene with the hydroxyl radical and the oxygen molecule, examines the mechanism of toluene conversion, shown in part in the figure below.



*Ab initio* (MP2, CCSD(T)), composite model chemistry (CBS-QB3, G4) and density functional calculations (M06 with the 6-31+G(d,p), 6-311++G(3df,2pd) and cc-pVQZ basis sets) were performed on reactants, intermediates, transition states and products of the  $C_7H_8$  + H0<sup>•</sup> reaction. The accuracy and precision of the methods were assessed by comparison to the experimental enthalpies of formation of several reactions intervening in the full mechanism. In the process, new enthalpies of formation are predicted for several radical and closed shell derivatives of toluene. The results point out towards a larger role than previously assumed for the benzyl radical. Several new routes are proposed, including one leading simultaneously to benzaldehyde and benzyl alcohol.

# **Session II.A**

# Supramolecular Chemistry

Chair: Giuseppina Luciani, University of Naples Federico II, Italy

## Structure of Water and Aqueous Solutions in the Ambient to GPa Pressure Range

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Liquid water is the most complex liquid on the Earth, e.g., the maximum density at 277 K, minima of isothermal compressibility and heat capacity at 319 and 273 K, respectively, with a tendency to diverse at around 228 K. All of the anomalies originate from hydrogen bonding. Various chemical processes in aqueous solution taking place in nature reflect the ion-water (ion hydration), water-water (hydrogen bonding), and ion-ion (ion association) interactions. For understanding the unique properties of water and aqueous solution and the underlying mechanism of chemical processes, thus, it is essential to investigate the solution structure at the molecular level over a wide range of temperature and pressure.

In the present talk, X-ray and neutron diffraction studies combined with an empirical potential structure refinement modeling (EPSR) on water and electrolyte solutions are reviewed. Energy-dispersive X-ray scattering at a laboratory and a synchrotron radiation facility (SPring-a) and neutron scattering at a pulsed neutron facility (J-PARC MLF) have been measured on water and aqueous solutions of sodium chloride, magnesium chloride, and calcium chloride at 300 to 523 K and several GPa. The experimental structure factors were subjected to EPSR modeling to reveal the structural properties of ion hydration and association and solvent water in terms of pair correlation function, coordination number, and 3-dimensional spatial density function. The orientational correlation of hydrated water molecules around the ions was also elucidated. The structural properties are discussed at the molecular level with respect to pressure, temperature, and ionic size.

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## Liquid Dense Clusters: Intermediate Phase between Nanocrystals and Single Molecules

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Liquid-dense clusters (LDCs) are formed by liquid-liquid phase separation, which is a process known for a long time in vitro as well as in vivo affecting a variety of nucleic acids, protein functions and metabolic pathways. Insights in the formation and dynamics of liquid dense clusters will open new options to optimize protein crystal growth, since they have been described as precursors for the nucleation in protein crystallization [1-2], will provide insights in the physical principle underlying the formation of membrane-less organelles in cells and functions within. Nonetheless, the knowledge about structural and dynamic properties of macromolecule LDCs of proteins and different nucleic acids remains by far incomplete (1). Insights about the folding state and packing of biomolecules inside LDCs will aid in understanding the relevance of metastable liquid-liquid phase separation, as well as understanding initial processes of protein aggregation, oligomerization and misfolding, e.g. in neurodegenerative diseases like Alzheimer, Parkinson, dementia and sclerosis [3]. In order to investigate formation and internal structure of liquid dense clusters (LDC) by coherent X-ray diffractive imaging, selected distinct proteins of high medical and biological relevance as well as RNAs were selected to prepare LDCs. The physico-chemical conditions for the formation, stabilization and labelling of selected macromolecule LDCs were established and systematically optimized. The influence of polyvalent ions and polyethylene glycols as precipitant agents, which can promote LDC formation, were investigated. A combination of single particle Brownian microscopy applying an ultrafast camera, in situ Dynamic Light Scattering as well as fluorescens and atomic force microscopy have been applied to follow the time resolved process of clusters formation. Initial results and data obtained were utilized to understand and to optimize the clusters formation, as well as assess their stability, also towards advanced X-ray imaging techniques. More detailed information about folding state and arrangement of macromolecules inside LDCs, particularly by using X-ray free electron laser based imaging will open new routes to utilize LDCs for structural investigation of nanomaterials and single macromolecules in a noncrystalline environment in the future, and will allow to prepare distinct nano- and microsized crystals, most suitable for serial diffraction data collection. Details will be presented.

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## Integrative Metallomic Approach to Uncover Metallo-Proteomes in Microbes: Novel Way to Overcome Antimicrobial Resistance?

## Sun H.,<sup>1</sup> Wang R.,<sup>1,2</sup> Wang H.,<sup>1</sup> Hu X.,<sup>1</sup> Yi-Tsun Kao R.,<sup>2</sup> Ho P-L.,<sup>2</sup> Li H.<sup>1</sup>

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It is crucial to identify metal-protein interactions at a proteome-wide scale which are difficult due to certain *weak* and *transient* interactions. We have developed an integrated approach consisting of gel electrophoresis and inductively coupled plasma mass spectrometry, LA-ICP-MS, IMAC, fluorescence and bioinformatics to identify metalassociated proteins using bismuth and silver as an example [1-5]. We have identified metal-associated proteins as well as to quantify the metals for rapid metallome/proteome-wide profiling of metal-binding proteins. Metal-tunable fluorescence probe can track metal-binding proteins in cells. We also show that an integrative metallomic approach together with metabolomics represents a powerful tool to uncover metallo-proteome in microbes as well as pharmacology of metallodrugs [2]. Development of new metalloagents to tame superbugs will be discussed [6].

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## Synthesis of Highly Functionalized 1,6-dihydropyridines via Zn(OTf)<sub>2</sub>-Catalyzed Three-Component Cascade Reaction of Aldimines and Two Alkynes (IA<sup>2</sup>-coupling)

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Although 1,4-dihydropyridines have attracted much more attention due to their wide biological and pharmaceutical applications, the biological applications of 1,2-/1,6- DHPs remained largely unexplored primarily because of the more challenging regioselectivity. For these reasons, the development of alternative methods for the selective synthesis of 1,2- or 1,6- dihydropyridines from readily available starting materials continues to be of intense interest.

Herein we describe a zinc(II) triflate catalyzed three component synthesis of 1,6dihydropyridines, involving aldimines, alkynes and electron deficient dimethyl acetylenedicarboxylate (DMAD), in good to excellent yields. Besides a range of different N-substituents, a variety of both aromatic and aliphatic alkynes could be used. The application of electron deficient propiolates instead of DMAD, gave rise to regiospecific incorporation of the ester functionality on the 1,6- dihydropyridine ring. The reaction proceeds via a cascade involving nucleophilic addition of the metal acetylide to the imine, followed by addition of the intermediately formed propargylic amine to the electron deficient alkyne and subsequent 6-*endo dig* cyclization.



# **Session II.B**

# **Computational Chemistry**

Chair: Daniele Licari Italian Institute of Technology (IIT), Italy

## II.B-1 - Key-Note Lecture

## New Avenues for Computational Chiral Spectroscopy

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Chiral spectroscopies are powerful techniques that allow the determination of the absolute configuration of a chiral sample, as well as provide additional detail and more specific insight into the sample's properties when compared to non-chiral measurements. From circular birefringence to vibrational circular dichroism, there is a wide array of available techniques depending on the property of interest. In almost all cases, in order to assign the absolute configuration of a sample from an experimental measurement, a theoretical calculation is required to determine the sign of the property associated with each enantiomer [1]. For this reason, several methods have been developed in the past to accurately reproduce the chiral response of molecular systems. Recently, we have expanded upon the available theoretical and computational techniques to simulate the emission of circularly polarized radiation of a system in a triplet state, a phenomenon known as circularly polarized phosphorescence (CPP) [2,3], and applied it to both organic and inorganic systems, of the type that has found applications in electroluminescent devices such as OLEDs, sensors, and probes. In addition, to provide a more profound insight into the chiral response, we revisited vibrational circular dichroism (VCD) [4] a well-known spectroscopy that exposes the chiral vibrational signature of a system. Thanks to recent developments both regarding the treatment of anharmonic effects [5] and in graphical visualization tools, we have expanded upon a visualization technique that can be used to truly expose the origin of the vibrational chiral response of a system by plotting the movement of the electrons during the vibration [6]. These efforts will be able to offer new and more accurate tools for the study of chiral systems through spectroscopy.

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### II.B-2

## Computational Characterization of the Herbicide Metolachlor: Structure, Conformational Analysis and Monohydroxylated Photo Degradation Products

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Electronic structure calculations have been performed for the characterization of the different con-formers of the herbicide Metolachlor (2-chloro–N-(2-methyl–6-ethylphenyl)-N-(2-methoxy-1-methylethyl) acetamide, MC, see Fig. 1), the radical structures obtained by the photo chemical breaking of the C-Cl bond and the most important, experimentally identified mono hydroxylated photo fragmentation products. Only the S-metolachlor enantiomer was considered, since it is the species showing herbicide activity. The goal of the study has been twofold.



Fig.1 - Structure of S-metolachlor, indicating the elements of symmetry

The first goal was to investigate the rotation of both the amidyl group and the substituted phenyl group, and to analyze the conformational pattern of both the neutral molecule and the corresponding radical species formed. Ten different con-formers were identified for the S-metolachlor enantiomer, all of which show an approximately perpendicular disposition of the amidyl and the phenyl planes. They were classified into two families of minima, depending on the orientation of the carbonyl group (either cis or trans with respect to the phenyl ring). All the minima in the S-cis family were found to lie well below those in the Strans family at the DFT M06/6-31+G(d,p) level. The free energy of isomerization for the lowest energy minima in both families was found to be  $\Delta G_{298}^{0}= 6.2$  kcal/mol, and they are separated by a barrier of 34.9 kcal/mol (in good agreement with the experimental energy of activation, 36.9 ± 3 kcal/mol). The second part of the work was devoted to study the most important isomeric forms of the metolachlor radical obtained through the photolytic cleavage of the C-Cl bond and the major photo degradation mono hydroxylated metabolites that arise from the coupling of the metolachlor radical with the OH radical. The reaction enthalpies for the various hydroxylation pathways have been calculated and based on these values, a theoretical justification of the significance of the various hydroxylation channels has been suggested. In particular, the importance of the phenyl group hydroxylation has been discussed.

Acknowledgements: ONV thanks economic support for this project from Pedeciba and UdelaR.

## II.B-3

## Hydrogen Bond Stability of Quinazoline Derivatives Compounds in Complex against EGFR using Molecular Dynamics Simulation

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Epidermal Growth Factor Receptor (EGFR) is the most frequent protein mutation in cancer and promising target to inhibit the cancer growth. In this work, stability of hydrogen bond as the main interaction in inhibition mechanism of cancer will be evaluated using molecular dynamics simulation. There were two compounds (T1 and T2) as new potential inhibitors that were complexed against the wild-type EGFR protein. The dynamics properties of each complexed were compared with respect to erlotinib against EGFR<sup>wt</sup>. The result revealed that both compounds had an interaction in the main catalytic area of protein receptor which is at methionine residue. Inhibitor T1 showed additional interactions during simulation time but the interaction tend to be weak. Inhibitor T2 displayed a more stable interaction. Following dynamics simulation, binding free energy calculation was performed by two scoring techniques MM/PBSA and MM/GBSA method and gave a good correlation with stability of complex. Furthermore, potential inhibitor T2 had a lower binding free energy as a direct consequence of the stability of hydrogen bond interaction.

### II.B-4

## Atomistic Modelling of Surfaces, Nanoparticles and Nanoalloys for Magnetism, Energy and Health Applications

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Complex materials such as thin films and nanoparticles, including nanoalloys, receive much attention because of their numerous potential applications in fields like metallurgy, catalysis, magnetism, optics and health. One main scientific challenge is to model their structure and properties as accurately as possible in order to participate to the design of new materials with targeted properties. In this lecture, a review of the methodological approaches to overcome such a challenge will be given. In particular, the modeling of realistic materials close to experimental conditions requires a multi-scale approach implying to go from ab initio methods to large scales atomistic simulations. This purpose will be illustrated within the presentation of combined ab initio and atomistic calculations applied to the characterization of metallic thin films, nanoparticles and nanoalloys together with some related properties of sorption and magnetism, two main phenomena leading to potential applications in energy and health fields.

# **Session III.A**

# **Inorganic Chemistry**

Chair: Hyunjoon Song KAIST, Korea

## III.A-1 - Key-Note Lecture

## How Copper Transport Systems Can Modulate the Efficacy of Platinum

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Cisplatin is the most important Pt-based drug used for the treatment of numerous human cancers including testicular, bladder, ovarian, head and neck, lung, and breast cancers [1].

Unlike platinum, endogenous copper is an essential trace element that provides numerous vital functions for human health and development. Cu homeostasis pathways exhibit high protein-protein specificity and involve Cu chaperones that bind and deliver the metal to sub-cellular targets. In humans, copper transporter 1 (CTR1) is the major Cu influx protein. The metallochaperone Atox1 transports Cu(I) to the metal-binding domains (MBDs) of two  $P_{1B}$ -type ATPases: the Menkes (Atp7a) and Wilson (Atp7b) disease proteins [2,3].

Several studies indicate that the copper transport machinery is also involved in the cellular response (sensitivity or resistance) to Pt anticancer drugs [4].

In this presentation, the most recent mechanistic insights into the cross-talk of cisplatin and Cu-trafficking proteins will be discussed [5-7].

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## Cooperative Effects of Atomic Ligands on the NMR Signals of [AX4] (A = C, Si, Ge, Sn, Pb; X4 = Combination of Four Halido and Hydridoligands) Coordination Compounds

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The study of the NMR chemical shift variations produced by mono atomic ligands bonded to NMR active central A atoms, in [ALn] compounds (A = C, Si, Ge, Sn, Pb, Pt; Ln = combination of n halido/hydrido ligands; n = 4-6) is of wide interest. In particular, we found that the observed central atoms  $\delta(13C, 29Si, 73Ge, 119Sn, 195Pt, 207Pb)$  NMR chemical shifts, are affected by both halido and hydrido ligands ionic radii and electronegativities overall sums,  $\Sigma(rL)$  and  $\Sigma(\chi L)$ , respectively. At this regard, we generally observed simple linear correlations between the central atoms  $\delta$  NMR chemical shifts and the  $\Sigma(rL)$ , when  $\Sigma(\chi L)$  results below a critical onset value. For instance, this occurs in several [AL4] coordination compounds, where the central A can show different oxidation states and geometries (octahedral, square-planar and tetrahedral). [1-3] Interestingly, in [CL4] and [SiL4] coordination compounds, we could determine a dependence of the  $\Delta\Sigma(rL)$  difference on  $\Sigma(\chi L)$ . Indeed, above the indicated onset value the example  $\Delta\Sigma(rL)C$  variations result directly proportional to the increase of  $\Sigma(\chi L)$ . Similar trends were also observed in the analogue Si derivatives.

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## Antitumor Effects Induced by the Promising Drug [Pt(0,0'-acac)(γacac)(DMS)] in *Cisplatin* Resistant Epithelial Ovarian Carcinoma Cell Line (SKOV-3): a <sup>1</sup>H NMR Metabolomic Study

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NMR-based metabolomic analysis of cells, tissues and biological fluids represents a helpful technique to assess drugs' tumour response and to explore the mechanism of action and resistance of drugs. [1]

In this work, a <sup>1</sup>H NMR metabolomic approach coupled with multivariate statistical analysis (MVA) were used to evaluate the pharmacological activity of the new promising Pt(II) complex  $[Pt(0,0'-acac)(\gamma-acac)(DMS)]$ , Ptac2S, on Epithelial Ovarian Carcinoma (EOC) cisplatin resistant cultured cell line (i.e. SKOV-3 cell line). Previous studies showed that Ptac2S is very interesting for its pharmacological activity shown in different in vitro cultured tumour cell lines, and in vivo. [2-3] The interactions of Ptac2S with nongenomic targets, which has been demonstrated in previous studies, [4] revealed a mechanism of action of this compound very different from *cisplatin*, although not completely clarified yet. For this reason, in order to get more detailed information about the mechanism of action of this new complex, Ptac2S, in this study, the metabolic variations of aqueous and lipidic SKOV-3 cells' extracts and the composition of the corresponding extracellular culture media induced by Ptac2S treatment have been compared to those of *cisplatin*. Based on our MVA (multivariate data analysis) results, the effects of Ptac2S and *cisplatin* on the SKOV-3 cells metabolome were shown to be significantly distinct. In particular, higher level of pyruvate were observed in Ptac2S treated with respect to *cisplatin* treated cells (in both aqueous and culture media) and a very different lipid expression resulted after the exposure with the two drugs (Ptac2S and *cisplatin*). The here proposed NMR-based metabolomics analysis confirms that Ptac2S limits cancerous cells proliferation, with a mechanism very different from that of *cisplatin* and essentially cytoplasmic, in according with previous studies. [2-4]

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# **Session III.B**

# **Theoretical Chemistry**

Chair: Andrea Melchior University of Udine, Italy

## Single-Ion Thermodynamics from First Principles. Absolute Hydration Free Energies of Alkali Metal Ions and Single-Electrode Potentials from *ab initio* QM/MM MD/TI Simulations

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Despite the tremendous success and importance of the field of thermodynamics as a main cornerstone of chemical and physical sciences, the properties of chemical species carrying an overall net-charge are not fully incorporated into the thermodynamic framework. The reason why single-ion thermodynamics still remains an active and highly challenging field of research is linked to the electroneutrality constraint inherent to all experimental setups at equilibrium. This limitation is associated with a number of thermodynamic parameters, with the re-anchoring of the series of electrode potentials onto an absolute scale (i.e. without the need of a reference such as the standard hydrogen electrode) being one of the most prominent examples. Due to its importance for chemical and physical research on a general scale and enormous effort dedicated to this research question for more than one century, the anchoring of single-ion thermodynamics via the absolute intrinsic hydration free energy of the proton  $G^{\circ}_{H+,hvd}$  still remains unresolved to date. This is not a consequence of inaccuracies in the individual measurements, but the result of different extra-thermodynamic assumptions (ETAs) employed by different researchers, which are often highly incompatible and cannot be verified based on the results of the respective measurements. As a consequence, the experimental estimates for  $G^{\circ}_{H+,hvd}$  cover a range of more than 250 kJ/mol and display no convergence when plotted against the year of publication. A highly promising alternative route to tackle this problem are theoretical approaches. Recently, six individual theoretical sub-fields (molecular mechanics MM, quantum mechanics QM, hybrid QM/MM, molecular dynamic MD, thermodynamic integration TI and continuum electrostatics CE) have been combined into a single QM/MM MD/TI simulation approach [1] to address this challenging topic *via* first principle calculations of absolute ionic solvation free energies  $\Delta G^{\circ}_{M+,hvd}$  in explicit solvent at a well-defined state point (T = 298.15 K, p = 1 bar). Despite the fact that the resulting hydration free-energies of three investigated ions (Li<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>) are found in the range from -525 to -343 kJ/mol, the associated estimates for  $G^{\circ}_{H+,hvd}$  are highly consistent (-1100 to -1096 kJ/mol, quantitative within error bars), being in remarkable agreement with one of the most thorough analyses of available experimental data recommending a value of -1100±5 kJ/mol.[2] In addition, the three associated  $\Delta\Delta G^{\circ}_{M+,hyd}$  values (*i.e.*  $Li^+ \rightarrow Na^+$ ,  $Na^+ \rightarrow K^+$  and  $Li^+ \rightarrow K^+$ ) are, too, in excellent agreement with experimentally accessible  $\Delta\Delta G^{\circ}_{M+,hyd}$  data.[2] Detailed analysis of the contributions to the QM/MM potential energy as well as the comparison of structural and dynamical data of the hydrate with experimental results confirm that a highly accurate description of the hydrated system is achieved with the employed QM/MM simulation strategy.

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## III.B-2

## **Kinetics of Electrodeposition with Diffusion-Controlled Growth**

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The theoretical description of the potentiostatic transient during electrochemical deposition is motivated by the possibility to understand the fundamental mechanism of a new phase formation, ruled by nucleation and diffusion-controlled growth, in dependence of overpotential. In the diffusion regime, island growth is controlled by the mass transport of the depositing ions to the island surface. Theoretical models have been proposed for describing the current density in terms of simultaneous and progressive nucleation along with two-dimensional (2-D) and three-dimensional (3-D) growth processes which have been profitably employing to interpret experimental chronoamperometric curves. Modeling island growth in the diffusional regime is an involved problem owing to the interference of diffusional fields of growing nuclei, namely of *correlation* effect on nucleus growth.

The present contribution focuses on island growth in electrodeposition, in the framework of "planar diffusion zones" and "3D nucleation and growth" approaches for simultaneous nucleation, where all nuclei start growing at the same time. Combination of both methods allows a more comprehensive description of the kinetics in terms of nucleus growth law, mean film thickness and surface coverage of the electrode, quantities that are not accessible using just one of these methods alone. In the case of progressive nucleation, where all nuclei are generated continuously as the transformation proceeds, we focus on the effect of *spatial correlation* of nuclei on current density that implies non-random distribution of nuclei. To this end stochastic approaches based on the use of correlation functions has been employed. The proposed approach provides a good approximation of the kinetics of both deposited material and electrode surface coverage. The development of theoretical models that properly take into account correlation effects during electrodeposition can be a valuable support to the controlled production of nanomaterials with efficient functionalities.

### III.B-3

## The Solvation Properties of Cu<sup>2+</sup> in Liquid Ammonia: an Ab Initio Quantum Mechanical Charge Field (QMCF) Molecular Dynamics Study

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The solvation of Cu<sup>2+</sup> in liquid ammonia has been investigated using ab initio quantum mechanical charge field molecular dynamics (QMCF-MD) simulation. The simulation box under periodic boundary conditions consisting of 1 Cu<sup>2+</sup> and 999 ammonia molecules. The temperature was set constant at 235.15 K with canonical NVT ensemble. The calculation method used Hartree-Fock with LANL2DZ-ECP and DZP Dunning basis set for the ion and ammonia molecule respectively. The trajectory was collected every fifth step during simulation time of 25 ps. The result of this simulation system formed two solvation shells. The maximum probability to find NH<sub>3</sub> ligands in the first solvation located at 2.23 Å, and others in the second solvation shell had high lability. The detailed analysis of coordination number distribution and angular distribution function were associated with stable tetrahedral, and the low stabilization energy of donor-acceptor ion-ligand in NBO analysis indicated that Cu<sup>2+</sup>-NH<sub>3</sub> formed an electrostatic interaction.

### III.B-4

## User-friendly Access to the Virtual Multifrequency Spectrometer

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The impressive advances of computer power, effective and user-friendly software and graphical interfaces are leading to the development of a new generation of virtual tools able to deal effectively with the complex systems and phenomena of current interest in the study of molecular systems.

Going from collections of numbers for oversimplified models toward vis-a-vis comparison between in silico and *in vitro* outcomes for real systems together with 3D renderings and natural interfaces should finally overcome the residual diffidence of experimentalists for computer simulations. Among those virtual instruments, we will be concerned here with the multifrequency spectrometer (VMS) our group is developing in the last few years [1,2], which allows vis-a-vis comparison of experimental spectra with their simulated counterparts, and interpretation of the results in all-in-one solution. Pre-and post-processing graphical tools were included for facilitating the use of the most advanced theoretical models for the former and improving interpretation of results for the latter.

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# **Session IV.A**

# Catalysis

Chair: Silvia Licoccia University of Rome Tor Vergata, Italy

## IV.A-1 - Key-Note Lecture

## Nanostructured Photo and Electrocatalyst Design for Chemical Energy Storage

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Renewable energy sources, mainly from sunlight, are the main themes of sustainable energy supply for a long time. The critical problem is, however, high volatility of energy resources dependent upon the weather and time. In order to maintain continuous supply, a reasonable energy storage system should be accompanied with the energy production Yet, the energy storage using electrochemical cells could not provide sufficient capacity as well as enough mass and volume densities of storage, therefore, many researchers consider another options based on the efficient conversion of solar energy into chemical energy using small molecules. Recently, carbon dioxide is of much interest as a mediator for this aim, due to its simple structure and high energy density per molecule. It is also beneficial to restore carbon cycles on earth.

There have been intense researches on direct conversion of carbon dioxide via photochemical, electrochemical and biological approaches. A photochemical method using sunlight in aqueous solution is regarded as an eventual approach, and recently, direct electrochemical carbon dioxide conversion is also attracting much attention, due to its high faradaic efficiency of various chemicals and simple device structure in a single batch. However, these reactions still need to be spent more than 10 years to be a commercial process, because of lack of knowledge on proper catalyst design. For instance, the most efficient photocatalysts reported thus far exhibited very low quantum efficiencies less than 0.04%. The development of new catalysts is definitely an indispensable prerequisite in this field.

In this presentation, we present the concept of "nanocatalyst", which has well-defined composition and morphology, to enhance catalytic performances in hydrogen generation and carbon dioxide reduction. We focus on the importance of catalyst morphology on photo- and electrocatalysts, and present some recent results of catalyst design, synthesis, and reaction study.

### IV.A-2

## A Kinetic Study of β-glucosidase Immobilized in Wrinkled Silica Nanoparticles

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In the past few years, the exploitation of lignocellulosic biomass has attracted great attention for its role in the production of biofuels and chemicals and its potential as a promising alternative, at low environmental impact, to reduce dependence on fossil fuel reserves. The enzymatic hydrolysis of cellulosic polymers and the consequent glucose fermentation to generate bioethanol is an ecologically sustainable and cost-effective process. In particular, the bioconversion of cellulose involves a set of enzymes, collectively referred to as cellulase.  $\beta$ -Glucosidase (BG) plays a key role in the enzymatic degradation of cellulose, hydrolyzing cellobiose to two glucose molecules, because cellobiose acts as inhibitor for the other cellulolytic enzymes.

In this work,  $\beta$ -glucosidase was immobilized by physical adsorption onto wrinkled silica nanoparticles, a recently synthetized mesoporous silica exhibiting both a central-radial pore structure and a hierarchical micro/mesoporous pore size distribution. The conformational analysis performed by FT-IR pointed out a preserved native conformation for the adsorbed enzyme. The catalytic performance of the bio-conjugate was evaluated by a kinetic study on the cellobiose hydrolysis. The immobilized BG had an apparent KM value slightly lower than the free enzyme, indicating an increased enzyme-substrate affinity. The biocatalyst was reusable four times without loss of activity. In conclusion, the current study resulted in the efficient entrapment of BG within nanoparticles with improved reusability, allowing the effective hydrolysis of cellobiose for biofuel production.

## IV.A-3

## Stimuli Responsive Microgel Containing Silver Nanoparticles with Tunable Optical and Catalytic Properties

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In this work, poly (vinylcaprolactum-co-itaconic acid) microgel was prepared by free radical polymerization. Silver nanoparticles were prepared in synthesized microgel networks by *in situ* reduction of Ag <sup>+</sup> ions which were loaded in microgel from aqueous solution of AgNO<sub>3</sub>. The prepared microgel was characterized by Fourier Transformation Infra-Red Spectroscopy, UV-Visible spectroscopy, Fluorescence Spectroscopy, X-Ray Diffraction, Laser Light Scattering, Thermal Gravimetric Analysis, Differential Scanning Calorimetry and Transmission Electron Microscopy. Swelling behavior of microgel was studied as a function of temperature and pH. The microgel was found to be in swollen state at low temperature and basic medium while in collapsed state at high temperature and acidic medium. A slight decrease in swelling capacity of microgel was observed after the fabrication of silver nanoparticles. A red shift was observed in surface plasmon resonance wavelength of silver nanoparticles with pH induced swelling of microgel. Catalytic activity of the composite microgel was studied by using them as catalyst for the reduction of 4-nitrophenol. Effects of temperature and catalyst dose were also investigated. Activation energy for the catalytic reduction of 4-nitrophenole was found to be 28.4 kJ/mol. The change in catalytic performance and shift in absorption maxima of composite microgel as a function of temperature and pH reveals that this system has potential to be used as tunable catalyst and optical sensor.

# **Session IV.B**

# Innovative Materials for Biomedical Applications

Chair:

Luigi Ambrosio Institute of Polymers, Composites & Biomaterials, National Research Council (CNR), Italy

## IV.B-1 - Key-Note Lecture

## **Grafting Strategy for Medical Applications**

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Multifunctional materials are promising biomaterials for circulating agents or prosthesis. For the former, we will present the elaboration of dendronized iron oxide for imaging sentinel nodes in cancer therapy [1] and the use of perfluoroalkyl phosphate to stabilize magnetic microbubbles [2]. For the latter, chemical and electrochemical graftings of PMMA chains onto a titanium large surface for reducing stress shielding will be presented [3].

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## IV.B-2

## Optimisation of Alkali Activation on Titanium to Grow PMMA Chains by Using ATRP for Biomedical Implants

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The necessity for biomaterials with bone-like mechanical properties in order to increase implant-bone compatibility led to the conception of a titanium-polymer composite material.

To create a strong interface, the two materials are attached through covalent bonds. To achieve this, the titanium surface undergoes a structuring alkaline (NaOH) treatment prior to the adsorption of a phosphonic acid-containing polymerization initiator. A polymer brush (Poly(methyl methacrylate), PMMA) is then grown from the modified titanium surface *via* controlled radical polymerization (ATRP) [2].

We present the multi-technique characterization of the titanium-polymer construct, infra-red spectroscopy, scanning electron microscopy imaging of cross-section obtained through cross-polishing, water contact-angle measurements and scratch-tests. In particular, we show that the preparation conditions of the titanate and of its subsequent chemical modification strongly influence the thickness, morphology and porosity of the polymer brush and must be controlled to achieve specific properties.

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### IV.B-3

## Anisotropic Mechanical Behaviour of Gelatin-PEG Hydrogel for Tissue Engineering

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Tissue engineering envisages concerted mechanical and structural behaviours of scaffolds similar to target tissue as well as enabling interactions with cells to regenerate or repair tissue. The mechanical properties of most polymeric materials are isotropic, as oppose to most soft tissues, which are anisotropic. Here, we create oriented big poresinterconnected small pores morphology in gelatin-poly(ethylene glycol) (G-PEG) hybrid hydrogel with controllable porosity, stiffness and anisotropy by simple uniaxial freezing. Compressive mechanical testing revealed elastic moduli of 0.33  $\pm$  0.04 MPa and 0.120  $\pm$ 0.03 MPa in the parallel and perpendicular direction to oriented porous macrostructure, respectively, with an associated anisotropy ratio of  $E_{\parallel}/E_{\perp}$  2.75. Cyclic compression experiment in both directions showed a good reversible behavior of the gels. We observed significant hysteresis that increased moderately with the applied maximum deformation. We also assessed the mechanical stability over time by incubating the samples in distilled water at physiological temperature up to one month. Finally, the time-dependant stress relaxation response of the gels was performed in both directions. Collectively, these results demonstrate that gelatin-PEG hybrid hydrogel could be engineered to closely mimic the anisotropic, elastic and viscoelastic behaviours of specific tissue.

## **Session V.A**

# **Pharmaceutical Chemistry I**

Chair:

Gian Maria Fimia National Institute for Infectious Diseases I.R.C.C.S. 'Lazzaro Spallanzani', Italy

### V.A-1 - Key-Note Lecture

### Discovery of Bioactive Drug Candidates from Some Turkish Medicinal Plants

### Sener B.

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Medicinal plants have an enormous potential for producing bioactive compounds of great benefit to mankind. There is a great scope for new drug candidates based on traditional medicinal plants throughout the world. The number of drugs derived from medicinal plants that are recently introduced into clinical use is increasing. Besides, numberous of standardized herbal extracts were approved by the health authorities to be used in phytotherapy as phytomedicines.

Turkey is one of the rich countries in terms of bioresources depends on different climates, geographical location, ecological factors and aquatic environments as well as the passageway between Europe, Asia and Africa. Therefore the floristic diversity provides a wide choice of species represented 12.000 taxa of which 3700 is endemic. Turkey is a party to the Convention on Biological Diversity which states that participating countries have sovereign rights over their own bioresources.

The drug discovery program from nature in our laboratory involves several steps from plant collection, extraction, HTS of the extracts by using *in vitro* enzyme inhibitory tests, bioassay-guided fractionation through the isolation, structure elucidation of bioactive compounds. We found diverse classes of compounds ranging from simple aromatics to complex molecules of alkaloids, terpenoids, steroids and phenylpropanoids showed significant biological activities including anticholinergic, anticholinesterase, antiinflammatory, antimalarial, antituberculosis and antiprotozoal from *Amaryllidaceae*, *Liliaceae*, *Iridaceae*, *Buxaceae*, *Fumariaceae*, *Taxaceae* etc. plant families. In this presentation, selected Turkish medicinal plants that possess several bioactivities alongwith some drug candidates have been summarized.

### V.A-2

### Angiotensin Converting Enzyme and HMG-CoA Reductase Inhibitory Activity of Philippine Plants

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In the Philippines, diseases of the heart are the number one leading cause of death according to the Department of Health. Coupled with the increasing obesity among young adults, the risk for atherosclerotic coronary heart disease is likewise on the rise. Research also linked cholesterol levels with the development of atherosclerosis.

Hypertension is a major health concern not just of the Philippine society, but it is a persistent problem worldwide. It is the 5<sup>th</sup> leading cause of morbidity according to the Department of Health's statistics. Untreated hypertension may lead to stroke, blindness, heart attack, kidney, and heart failure.

This research evaluated anti-hypertension and cholesterol-lowering activity of various plant extracts in search for leads in the development of new drugs.

#### V.A-3

### Structure Activity Relationship of 7-Hydroxy Betunolic Acid Against Staphylococcus aureus and MRSA

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Antibiotic-resistance crisis has become one of major public health problem in all over world and necessity of discovering new antimicrobial agents is greater than ever. The biggest challenge faced by the global drug industry today is finding the alternatives to the spiraling high cost and serious side effects associated with modern medicine. Bioavailability and safety consumption of triterpenoids by human for their diet as well as medicine for many eras without apparent ill effect, they can be considered as good of scaffolds for synthesis new derivatives as antibiotics. source (1R,3aS,5aR,5bR,7R,7aR,11aR,11bR,13aR,13bR)-7-hydroxy-5a,5b,8,8,11a pentamethyl-9-oxo-1-(prop-1-en-2-yl)icosahydro-1H-cyclopenta[a]chrysene-3a-carboxylic acid, (7hydroxy betunolic acid), is a triterpenoid which can be easily isolated from bark of Schumacheria castaneifolia which is endemic to Sri Lanka. This compound has shownantibacterial activity against both Staphylococcus aureus (ATCC 29213) and methicillin-resistant S. aureus, MRSA, (MIC 16 µg/ml). During this study structural analogues of 7-hydroxy betunolic acid (CBN-KTL, HYDX-OXN, ACD-EE, OLF-HDYN and OLF-HYB) were formed by modifying the carbonyl, hydroxyl, carboxylic acid and olefin groups at C<sub>3</sub>, C<sub>6</sub>, C<sub>17</sub> and C<sub>20</sub> positions to obtain ketal, ketone, ester and alkane as well as hydroboration product respectively. Their chemical structures were confirmed with spectroscopic data and antibacterial activity through broth micro dilution assay against S. aureus and MRSA. Results showed that all the modifications have increased the MIC values above the tested range (128 µg/ml) except HYDX-OXN (MIC 64 µg/ml).This indicates that the carbonyl, carboxylic acid and olefin groups at C<sub>3</sub>, C<sub>17</sub> and C<sub>20</sub> positions are highly important for the antibacterial activity.

#### V.A-4

## Osteoarthritis and Its Management Through Ayurvedic Drugs: A Novel Approach

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**Background**. Osteoarthritis which is also known as osteoarthritis or degenerative joint disease is aprogressive disorder of the joints caused by gradual loss of cartilage and resulting in the development of bony spurs and cysts at the margins of the joints. The name osteoarthritis comes from three Greek words meaning Bone, Joint and inflammation. According to WHO, Osteoarthritis is the second commonest musculoskeletal problem in the world population (30%) after low back pain. In India it is as high as 12% and India has the second largest Osteoarthritis patient base around the world.

**Materials and methods**. A clinical study involving 60 patients of Osteoarthritis was done at Governmentayurvedic College, Department of Kayachikitsa, to study the efficacy of an oral poly-herbo mineral compound and the effect of Aswagandha Grita Basti – a traditional ayurvedic enema therapy.

**Results**. The results of the study showed that the effect of oral poly-herbo mineral compound andtraditional therapy is effective in controlling pain, restricted movement, swelling, morning stiffness and crepitus. Statistical analysis of the effect of the trial drug on the subjective parameter of pain showed that after 90 days of treatment the initial mean $\pm$  SD of 2.1 $\pm$ 0.12 was reduced to 1.08 $\pm$ 0.39, with a Z value of 11.33, which is statistically significant at (p=  $\leq$  0.01). Assessment of overall result was found to be as markedly improved in 43.33% and moderately improved in 55% of the patients under study.

## **Session V.B**

## **Chemical Technologies for Life Science I**

Chair: Adele Carradò Université de Strasbourg, France

### Design and Application of Novel Materials Containing Nanoparticles with Controllable Photo-Thermal Properties

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Nanoparticles with absorption in Near-Infrared (NIR) region, that display efficient photo-thermal conversion of NIR light, are under great attention due to wide applications opportunities in nanomedicine. This phenomenon is intensively being studied for cancer therapy (localized hyperthermal cancer cells ablation) together with photo-thermally induced drug release approaches, new quantitative biochemical analysis, and cells stimulation. In present study, a range of photo-thermally active nanoparticles with intense absorption in NIR region (700-1100 nm) were synthesized and applied to fabricate inkjet-printed surfaces or to be incorporated into thin polymeric films. For each type of sample the parameters affecting on photothermal effect, such as laser power and wavelength, nanoparticles concentration, printing parameters etc., were studied in details. All printed patterns showed a significant photo-thermal effect under NIR irradiation. The cytotoxic studies indicated low toxicity of printed surfaces. In addition, the NIR-triggered release of molecules from printed surfaces was studied. These preliminary results suggest the way of the development of a new class of low-cost, disposable and smart devices for localized thermal treatments combined with temperature triggered drug release. The fabricated polymeric films containing nanoparticles displayed also pronounced photo-thermal effect depending on light intensity and the nanoparticle distribution in the films. All films displayed rapid ( $\approx 15$  s) increase of temperature turning to plateau when irradiated, and a subsequent rapid (≈10 s) decrease to initial temperature when the irradiation is switched off. Prolonged and repeatable irradiation exposure did not cause any changes in photo-thermal response. The obtained results together with preliminary in-vitro and ex-vivo studies suggested promising application of fabricated materials for cellular and topical applications. Moreover, the local photo-thermal effect triggered by NIR irradiation of resulted films was found to be highly efficient in killing bacteria, therefore providing additional application opportunities.

## Synthesis, Characterization and Interaction Studies of Smart Nano Carriers as Delivery Systems for Cancer Therapy

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The focus of the present work is the preparation of two type of nano carrier as delivery systems for cancer therapy, new metal-based nano drug (i) and inorganic nano crystals (ii), to overcome the limitations of chemotherapy such as poor water solubility of most common chemotherapeutic drugs. The Pt complex derivatives, have been synthesized at nano-size by ultra-sonication method, whereas CaCO<sub>3</sub> nanocrystals have been synthesized by Spray Drying process. Both systems were characterized by dynamic light scattering (DLS), transmission electron microscopy (TEM) and scanning electron microscopy (SEM), in order to evaluate the stability during time. The interaction of the nano carriers with HSA have been investigated under physiological conditions by a series of experimental methods. The *in vitro* interaction against the human carcinoma cell lines was evaluated by MTT assay and cytofluorimetric analysis. Confocal microscopy was used to monitor cell interaction and cellular uptake. We have further investigated the interaction nature and release mechanism of drug loaded/released within/from the nano carriers using the IcP analysis for metal-based nano drug, and an alternative approach based on liquid chromatography coupled to mass spectrometry for inorganic nano crystals. Our approach provides a good loading efficiency for both systems prepared. The results of *in vitro* studies indicate that the our nano systems have excellent biological activity against cancer cells. Furthermore, preliminary results on *in* vivo model, Drosophila Melanogaster, were shown to learn the detriment caused by nanoparticles.

### Surfactant-based Nanocarriers

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Efficient and safe drug delivery has always been a challenge in medicine. The use of nanotechnology, such as the development of nanocarriers for drug delivery, has received great attention owing to the potential that nanocarriers can theoretically act as "magic bullets" and selectively target affected organs and cellswhile sparing normal tissues. During the last decades the formulation of surfactant vesicles, as a tool to improve drug delivery, brought an ever increasing interest among the scientists working in the area of drug delivery systems.

Niosomes are self-assembled vesicular nanocarriers obtained by hydration of synthetic surfactants and appropriate amounts of cholesterol or other amphiphilic molecules. Just like liposomes, niosomes can be unilamellar or multilamellar, are suitable as carriers of both hydrophilic and lipophilic drugs and are able to deliver drugs to the target site. Furthermore, niosomal vesicles, that are usually non-toxic, require less production costs and are stable over a longer period of time in different conditions, so overcoming some drawbacks of liposomes. The niosome properties are specifically dictated by size, shape, and surface chemistry which are able to modify the drug's intrinsic pharmacokinetics and eventual drug targeting to the areas of pathology. In particular, niosomes can be useful in brain delivery as polysorbates can act as an anchor for apolipoprotein E from blood plasma. The particles mimic LDL and interact with the LDL receptor on Blood Brain Barrier (BBB), leading to the endothelial cells uptake. Furthermore, to overcome the drug low capability to cross BBB a non-invasive intranasal delivery system, chitosan coated niosomes, was developed.

Focused Ultrasound-mediated drug delivery, a technique that offer a unique noninvasive venue to deliver drugs to the brain through transient opening of the BBB by using of ultrasound in combination with gas-filled bubbles. New carriers, the "Bubblesomes", with a gas core coated by a surfactant bilayer, able to combine the characteristics of a drug carrier and a contrast agent (theranostic system)were developed When focused ultrasound is applied in presence of drug loaded nanobubbles intravenously administered, inertial cavitation is induced, due to the rapid expansion and violent collapsing of bubbles. This can cause the temporal and fully reversible opening of BBB due to the enhanced endothelial porosity and vascular permeability phenomenon called sonoporation, resulting in an increased drug uptake. It is evident that since Niosome early introduction to cosmetic industry in the late '70s, their role has diversified to other application areas and they are now being ardently explored as potential carriers for sustained and targeted drug delivery.

### Nanocoaxial Arrays for Electrochemical Detection of Disease Biomarkers

### <u>Naughton M.J.</u>, Archibald M.M., Chiles T.C., Burns M.J. Boston College, Chestnut Hill, MA 02467 USA naughton@bc.edu

Sensitive, real-time detection of biomarkers is of critical importance for rapid and accurate diagnosis of disease for point of care (POC) technologies. Few current methods allow for POC applications due to limitations including sophisticated instrumentation, high reagent consumption, limited multiplexing capability, and cost. Here, we report a novel nanoscale 3D platform that offers utility in sensitive and selective electrochemical detection, as well as in nanophotonics,[1] photovoltaics, [2] and neuroelectronics. [3] The device architecture is composed of vertically-oriented, nanoscale coaxial electrodes in array format (~10<sup>6</sup> coaxes per square millimeter). As an electrochemical sensor, we have demonstrated significant increase in sensitivity relative to conventional planar controls, [4] and the detection of bacterial toxins using an electrochemical ELISA and differential pulse voltammetry. [5] In addition to matching the detection profile of standard ELISA, the nanocoax array provides a simple electrochemical readout and a miniaturized platform with multiplexing capabilities for the simultaneous detection of multiple biomarkers, giving the nanocoax a desirable advantage over the standard method towards POC applications.

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## **Session VI.A**

# **Pharmaceutical Chemistry II**

Chair: Bilge Sener Gazi University, Turkey

### **Emerging Alternative Medicine for Diabetes**

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Medicinal plants are widely used against diabetes throughout the world and as well as in Pakistan. But, few of them have validated for scientific criteria, great diversity of animal models are being introduced to better understand the pathogenesis and new drug effects of diabetes. Diabetes mellitus is rapidly growing at an alarming rate. The attention is focussed to work on previously unexplored medicinal plants (such as Boerhavia procumbens, Corchorus depressus, and Farsetia hamiltonii) extracts from Choilstan Desert of region Bahawalpur in a standard scientific and systematic way. These medicinal plants are being traditionally used to cure devastating diabetes mellitus. The crude extracts would be subjected to a screening study to detect potential anti-diabetic activity. Our experimental strategy involves collection of medicinal plants from the Cholistan Desert of Bahawalpur in different season. Consequently, chemical fingerprinting (bioassay-guided extraction, fractionation, purification and structural characterization of lead compounds through modern spectroscopic techniques) and biological fingerprinting (DNA-target analysis, HSA binding, or liposome-binding chromatography) have been under taken. Finally, studies also include toxicological profiling; followed by pre-clinical trials to cure diabetes in alloxan/streptozotocin induced diabetic rats.

## On the Inhibition Mechanism of CTX-M-15 Serine Hydrolase by Avibactam: a Theoretical Approach

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The resistance to  $\beta$ -lactamic drugs developed by clinical bacteria is usually mediated by the production of one or more hydrolytic enzymes, known as  $\beta$ -lactamases, which inactive the antibiotic by hydrolyzing the amide bond of the  $\beta$ -lactam ring. A successful strategy to face the resistance mechanisms has been to combine a  $\beta$ -lactam antibiotic with a  $\beta$ -lactamase inhibitor. Avibactam is a non- $\beta$ -lactam-based inhibitor showing promising results against class A and C serine hydrolases. Despite of the number of articles published in literature, certain aspects have not been clearly elucidated, mainly those related with the activation of serine.

In this contribution the inhibition mechanism of CTX-M-15 class A serine hydrolase by the inhibitor avibactam is addressed by a combined molecular dynamics (MD) and quantum mechanics / molecular mechanics (QM/MM) approach postulating a novel hypothesis stating that the residue Ser70 is the sole reacting residue, *i.e.*, itself may play the role of the acid-base species required for the enzyme inhibition. Other residues located in the active site have key participation in the positioning of the inhibitor in the right conformation to favor the attack of Ser70, in addition to the stabilization of the transition state by electrostatic interactions with avibactam. The results validate the hypothesis and show that the reaction follows an asynchronous concerted mechanism, in which the nucleophilic attack of the hydroxyl oxygen of Ser70 precedes the protonation of the amidic nitrogen and ring opening. The calculated activation barrier is 16 kcal/mol in agreement with the experimental evidence.

### Lipoxygenase Inhibitory Activity of Philippine Terrestrial Plant Extracts

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The Philippines is one of the 17 countries that contain two-thirds of the entire biological diversity of the Earth with more than 20,000 plant species, and about a third of it endemic. This presents a vast ground for the discovery of novel plant-derived bioactive agents for various diseases that plague the world. Inflammation is one of the many mechanisms by which the body responds to any type of injury and is most often accompanied by pain. Lipoxygenases are the key enzymes in leukotriene biosynthesis and catalyzes the initial step in the conversion of arachidonic acid into leukotrienes that are considered potent mediators of inflammatory and allergic reactions. Inhibiting lipoxygenases are possible targets in treating various inflammatory diseases. A total of 54 plants, reported in the literature to have anti-inflammatory activities, were screened for their ability to inhibit 15-lipoxygenase from *glycine max*. The spectrophotometric assay used is generally based on the 15-LOx catalyzed reaction between oxygen and a polyunsaturated fatty acid, linoleic acid. The reaction of linoleic acid and 15-LOx leads to the formation of 13-S-hydroperoxyoctadecadienoic acid (13-HPODE), which is hydrolyzed into 13-S-hydroxyoctadecadienoic acid (13-HODE) which can be detected at 234 nm. Out of the 54 plants tested, 12 were found to be active belonging to the following families: Anacardiaceae, Tiliaceae, Betulaceae, Sapotaceae, Caesalpinaceae, Umbelliferae, Annonaceae, Lauraceae, and Myrtaceae. The results of this study reinforces the ethnopharmaceutical use of these 12 plants in treating inflammation, particularly in the lipoxygenase biochemical pathway. Further studies are being done in order to identify the active components of these bioactive plants.

### Polyphenolic Composition, Antioxidant Capacity and Volatile Compounds of *Phoenix dactylifera* L. var. Ajwa

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The excessive formation of Reactive Oxygen species (ROS) due to any abnormal stimuli impart deleterious effects on the internal cellular environment. Natural products being rich in various bioactive compounds used to provide broad range of protection against these reactive oxygen species. *Phoenix dactylifera* var. Ajwa, is amongst the best dietary sources of natural compounds which is equally beneficial, both nutritionally and economically. Because of its exceptional antioxidant properties, it grab the attention of nutritionist and natural product scientist to further probe on the spectrum of efficacy against the cellular oxidative damages. This research aimed to study the combine effect of Ajwa date fruit and seed extracts on total polyphenol content and free radical scavenging activity through various *in-vitro* and *ex-vivo* antioxidant assays with identification of bioactive compounds through GCMS. In the present study the total phenolic and flavonoid contents were found to be 993mg-5020mg and 163mg-907mg as GAE/100g and RE/100g respectively. DPPH scavenging assay was represented in terms of Ascorbic Acid and Trolox equivalent, i.e., 4.293-26.910mM AAE/100g and 4.637-28.317mM TEAC/100g respectively. While ABTS decolorizing assay was observed in the range of 9.61-29.18mM TEAC/100g. Moreover, Beta-carotene assay revealed that combination extract prevent the oxidation of beta-carotene in the range of 27.76-69.14%. Oxidative hemolysis inhibition assay on HRBCs showed that methanolic extract was more potent followed by ethyl acetate extract, *i.e.*, 93-94% inhibition has been shown. GCMS studies of extract mixture revealed several important chemical constituents such as Methyl hexadecanoate (42%), Hexadecanoic acid (32%), Ethyl Hexadecanoate (32%), Methyl (E)-9-dodecenoate (30%), Methyl cis-11-octadecenoate (56%), Methyl 9,12-octadecadienoate (28%), Methyl (E)-9-Octadecenoate (67%), (Z,Z)-9,12-Octadecadienoic acid (34%), Cholestan-22(26)-epoxy-3,16-dione (9%), Ethyl isoallocholate (5%), Ergost-5-en-3-ol, acetate, (3β,24R) (7%), Stigmastan-3,5-diene (19%),  $\alpha$ -Tocopherol (27%), Lup-20(29)-en-3 one (3%), Stigmast-4-en-3-one (17%) Stigmasta-5, 22-dien-3-ol, acetate-(3β) (11%), Stigmast-5-en-3-ol, (3β, 24S)- (35%) and Stigmast-5-en-3-ol, Oleate (2%). In addition, in the above listed compounds found in Phoenix *dactylifera* some of them showed bioactivity as per literature, which might be further explored to work out for their prominent role in combating cardiovascular & other disorders. Further, such exploration may also be useful for the nutraceutical and pharmaceutical industries to develop commercial products based on natural compounds for the maintenance of cardiovascular health & various ailments.

## **Session VI.B**

## **Chemistry for Nanomaterials**

Chair: Maurizio Peruzzini National Research Council (CNR), Italy

### VI.B-1 - Key-Note Lecture

### Challenges and Opportunities of Energetic Materials for Industry

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With an unprecedented rise of the global temperature and concern for the consequent climate change, the energy sector is facing several important issues. To reach the targets set by the Paris Agreement is therefore paramount to reduce the CO<sub>2</sub> emissions, main responsible for the greenhouse effect. In order to do so, it is important either to push the wide spreading of the renewables and improve the efficiency of the traditional processes.

Chemistry plays a vital role to design materials able to improve the devices' reliability, stability and efficiency. The talk will consider the role of chemistry in developing some key technologies for the transition towards a carbon neutral economy: the sunlight conversion (PV and solar fuels), solid oxide fuel cells (high efficiency conversion of fuels into electricity) and energy storage.

In all these applications is fundamental to consider, other than the efficiency, also the possibility to use not critical raw materials (noble metals or rare earth) and processes able to cope with the industrial needs of economy and reliability.

The talk will prove that a suitable chemical engineering of the starting materials and shaping processes can greatly improve the efficiency of these devices reducing at the same time also the production costs.

### VI.B-2 - Key-Note Lecture

### Molecularly Imprinted Nanoparticles Used in Competitive Pseudo-ELISA for the Detection of Toxins in Water

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In last years, harmful algal blooms (HABs) have increased its natural abundance in aquatic environments, due to eutrophication of water resources, producing numerous species of cyanotoxins such as anatoxins, cylindrospermopsins, saxitoxins and microcystins. Currently, numerous analytical techniques have been employed for the determination of toxins, including the use of immunoassays. Consequently with this, the numbers of commercial immunoassay kits have increased. However, the immunoassays use antibodies, which need special procedures for its production and use, presenting disadvantages such as high cost and time-consuming. For these reasons, molecularly imprinted polymeric nanoparticles (nanoMIPs) have been studied for use as plastic antibodies in immunoassays, specifically, in the enzyme-linked immunosorbent assay (ELISA). In this context, the main goal of this study was developed a competitive pseudo-ELISA for detection of Microcystin-LR (MC-LR) and an analogous of Domoic Acid (DA) in water. For that, polymeric nanoparticles based mainly on Acrylamide (AM) and Acrylic Acid (AA) were obtained via solid phase synthesis method and characterised by Dynamic Light Scattering (DLS) and Transmission Electron Microscopy (TEM). The obtained nanoMIPs were evaluated in the ELISA for different synthetic and real water samples. The nanoMIPs employed in the competitive assay presented high selectivity, demonstrating the potential in the determination of toxins in water, avoiding the use of antibodies. This assay was capable to detect concentrations of toxins in drinking and lake water samples. This modified bio analytical technique had high importance and can be an excellent tool for a rapid, sensitive and accurate detection of toxin in water bodies eutrophized.

**Acknowledgements:** Pereira E, thanks FONDECYT project No. 1160942 and Garcia Y is grateful for the scholarship CONICYT No. 63140157.

#### VI.B-3

### Chemical Engineering Valorization of Agro-Wastes from Pineapple Cultivation

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Cellulose fibers are high-performing fibers that have unique properties such as abrasion resistance, moisture absorbency, etc. enabling them to find usage in applications such as apparel, home textile and industrial. The production of premium quality fibers and greater use of cellulose fibers in place of cotton present several market growth opportunities. The production of man-made fibers involves the industrial processing of wood pulp derived from botanical sources, but fluctuating price of wood pulp is a major problem in this market that causes a shift of focus towards producing cellulose fibers from renewable sources. Industry trends indicate that the global market for textiles will focus greatly on biodegradable, eco-friendly, and skin-friendly fabrics, focusing towards investment for the implementation of new technologies and materials to produce new and high-quality products. For all these reasons, the companies are extensively into research and new product developments. This theme is strictly connected to the concept of sustainable economy achievable by the introduction of environmental friendly processes, by the study of new materials obtainable from renewable sources and by the exploitation and minimization of by-products and wastes from industrial processes. The biorefinery concept matches all these aspects: in a biorefinery biomass conversion processes are integrated and value-added chemicals, new materials, fuels, power, heat, can be obtained in a sustainable way with environmental friendly processes.

An interesting example is the case of Thailand, where agriculture and textile industry are working together to exploit the resources obtainable from pineapple cultivation. This nation produces over 2.2 million t/y of pineapple fruits; connected to this cultivation, recently, is developing a new business resulting from the extraction of fibers from leaves (PALF), to be employed with great potential in the textile sector. These fibers are obtained from the leaves of the plant Ananas comosus, which belongs to the Bromeliaceae family; they contain fibers  $(2.5 \div 3.5 \%)$ , pentosans (17.8 %), lignin  $(4.2 \div$ 12 %), fat and wax (3.3 %) and pectins (1.1 %). The presence of other constituents than fibers constitutes an impurity that needs to be removed, in particular lignin that acts as a glue for the fibrillar structure of the fibers, is responsible of the non-wettability and consequently of the non-dyeing of the fibers. PALF fiber is silky, fine and has interesting textile properties, is capable of blending with jute, cotton, ramie and some other synthetic fibres: so it can capture an important position among natural fibers as potential commercial grade textile fiber. In consideration of its properties, PALF is placed between jute and cotton or jute and ramie. This study proposes the development of an industrial process for extraction of fibres and exploitation of other constituents (mainly lignin and pectins), in order to reach a sustainable and economical profitable production process.

## **Session VII.A**

## **Proteomics and Metabolomics I**

Chair: Benedetta Mattei University of L'Aquila, Italy

### VII.A-1 - Key-Note Lecture

## Metaproteomics and Gut Microbiota: the Functional Scaffold Beyond the Genomes in Pre-Clinical and Clinical Applications

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The relationship between a healthy organism and its gut microbiota has not yet been completely understood, but a number of evidences have been already shown in the last decade on the relationship between host and bacterial genomes.

Murine models can assist in the description of the impact of either maternal milk or parental genetic background on the composition of the gut microbial populations in the first years of life.

A metaproteomic approach on such complex environments is always a big challenge that requires a strong effort in both data production and computational analysis, and the development of specific multitasking bioinformatics pipelines.

Herein we present LC-MS/MS based investigations on mouse gut microbiota in the early life, aiming at characterizing its functions and metabolic activities, beside a taxonomic description in terms of operational taxonomic units (OTUs). We present a quantitative evaluation of bacterial metaproteins, putting differential expression results in relation with functional and taxonomic classifications, particularly with proteins from orthologue groups, reducing the bias coming from the presence of a high number of shared peptides and proteins, among different bacterial species. We also discuss evidences on host proteins, revealing a modulated response in the mouse mucosal proteome in the presence of a different microbiota OTUs composition.

From pre-clinical to clinical models, we also present an application of metaproteomics pipelines to an extra-intestinal disease-microbiota profile such as the autism in paediatric ages.

Host co-correlations and microbiota dynamics are discussed in term of functional drivers of microbiota genetic patterns.

### **Proteomic Analysis of Host-Parasite Interactions**

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Pathogen interact with host proteins to either suppress or hijack host functions. Identification of protein-protein interactions is critical for understanding the biology of infection and point to novel targets in treatments against human pathogens. Hepatitis C virus (HCV) is highly efficient in establishing a chronic infection, having evolved multiple strategies to suppress host antiviral responses. HCV NS5A plays an important role in viral replication, in viral particle assembly and in preventing the antiviral response. Lacking enzymatic activities, NS5A function relies on its ability to interact with a variety of cellular proteins and to exploit host machineries to accomplish HCV life cycle. To gain insight the function of NS5A, we analysed NS5A interacting proteins by means of an affinity chromatography/mass spectrometry-based approach. In this screening, we found that the mitochondrial leucine-rich pentatricopetide repeat-containing protein (LRPPRC) binds to NS5A and is required for the efficient HCV replication. Since mitochondria are critical platforms for triggering the innate immune response, we investigated the possible involvement of LRPPRC in antiviral signaling. We found that LRPPRC interacts with MAVS (mitochondrial antiviral signaling protein) and negatively regulates the MAVS-mediated interferon response. Consistently with its ability to bind LRPPRC, we found that NS5A is able to repress MAVS activity and the interaction with LRPPRC is required for its inhibitory activity. Altogether, these results point out an important role of LRPPRC in controlling the antiviral response and highlight a novel mechanism by which HCV hijacks host factors to allow efficient infection.

## Characterization of Regulative Ubiquitination Mediated by TRAF6 During Autophagy Response

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Autophagy is a cellular process activated in stress conditions and tightly regulated by post-translational modifications (PTMs) to rapidly ensure cell survival. The kinase triad MTOR, AMPK and ULK1 is well characterized in regulating the phosphorylation state of a plethora of proteins involved in the activation of the autophagic machinery. Recently, also ubiquitination is emerging as PTM involved, not only in the specific recognition of substrates subjected to degradation by autophagy, but also as a key signal to modulate both stability and activity of proteins directly involved in the regulation of the autophagy response. In particular, TRAF6 is a E3-ubiquitin ligase involved in the positive regulation of autophagy through the activation of several autophagy-related proteins (e.g. BECLIN1 and ULK1) by mediating poly-K63 linked ubiquitination. Combining *in vitro* ubiquitination assay and innovative MS-based methods, we were able to identify lysines specifically ubiquitinated by TRAF6 on known and novel proteins involved in autophagy activation, thus giving a new tool for the identification of ubiquitinated site and increasing the chances to modulate autophagy response by interfering the TRAF6-mediated ubiquitination process.

## **Session VII.B**

## **Biomaterials - Nanomedicine**

Chair: M. I. Choudhary University of Karachi, Pakistan

### VII.B-1 - Key-Note Lecture

### **Advanced Biomaterials for Tissue Engineering**

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Modern medicine is based on the implementation of a personalised approach together a less invasive surgery for the restoration of human tissues and organs. Nature-inspired material science can be considered as the last frontier in biomaterials research. Indeed, the design of complex structural architectures from sub-micronic to nanometric dimensional scale allows geometrically and topologically mimicking the native state of extracellular matrix and its complex supramolecular assemblies. Biopolymers, biocomposites, nanofibrous & gel scaffolds could be used to mimic the fibrillar structure of ECM, and provide essential cues for cellular organization, survival and function.

In tissue repair/regeneration advanced routes and technologies are in progress to synthesize/process instructive biomaterials with biologically recognized functionalities. Among them, additive technologies such as 3D Printing is emerging as highly flexible process to design biomaterials able to mimic 3D ECM-like platforms and personalized structures for tissue repair/regeneration processes.

It has been shown that the use of minimally invasive surgery to treat bone defects has significant clinical potential. To achieve the ideal properties of bone filler, *i.e.* osteoconduction, osteoinduction and ease handling, specific compositions based on natural and synthetic polymers, ceramics, and composites have been developed. Here, advances in the synthesis, design and fabrication of 3-dimensional scaffolds and structures to guide regeneration processes in the skeletal system (*i.e.*, bone, IVD, nerve, skeletal muscle) will be presented.

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### VII.B-2 - Key-Note Lecture

## Functionalization of Polymers and Surfaces: a Way to Get Specific and Controlled Host Response Towards Implantable Medical Devices

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Polymers able to mimic biomolecules can be synthesized by various simples or complexes polymerization reactions or obtained by functionalization of macromolecular chains or networks. Several examples showing the interest of such chemistry on the improvement of biological responses will be described.

In addition, the mechanism at the origin of the biological activities will be demonstrated and related to the chemical composition of the mimicking biomolecules.

It is worth noting that the number and the distribution of the chemical groups along the macromolecular chains contribute to the specificity of interactions between surfaces and biological entities.

The improved understanding of the ways the copolymerization or the statistical functionalization of macromolecular chains could endow materials with specific biological properties helped to extend the endowment of the biological properties of polymers to those of implantables medical devices.

Different methods of grafting – "grafting from" and "grafting to" - bioactive polymers on polymeric and metallic materials and the observed biological *in vitro* and *in vivo* responses will be described.

#### VII.B-3

## Designing of Small-Molecule-Druggable Chemical Space - *Examples of* the Lead Discovery for Obesity, Multi Drug Resistance and Diabetes

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The growing demand for access to libraries of small molecules for high-throughput screening (HTS) has presented challenging opportunities in molecular library development which ultimately serve to uncover molecular leads as potential therapeutic agents aimed at improving human health. To accomplish this, it is necessary to develop new and innovative chemical methods, which ultimately can be used for efficiently generating libraries of new and novel structures. Despite significant advances, only a minute fraction of theoretical chemical space has been mined, potentially leaving large portions untargeted. Due to the expansive number of potentially "druggable" molecules, guided efforts are necessary. With this need in mind, we aimed to design and construct libraries of new heterocycles, with an emphasis on Lipinski's drug like characters such as less than 5 hydrogen bond donors, less than 10 hydrogen bond acceptors, less than 500 molecular mass. In addition to this we have emphasized on the synthesis of the bioactive heterocyles, such as reversal of multi-drug resistance in *S. aureus* and *coli*, anti-diabetes, anti-obesity, anti-ulcer and etc. Prominent libraries of compoundssynthesized and their biological activities obtained through this research work will be presented during the presentation.



o-Glucosidase Inhibition IC<sub>50</sub>~ 23.5±0.9 μM Acarbose (Standard) IC<sub>50</sub>~ 840.0±1.73 μM  $\begin{array}{l} \textbf{Anti-Adipogenesis}\\ IC_{50}=740.00\pm2.36\ nM\\ Curcumin\ (Standard)\\ IC_{50}=18.62\pm0.74\ \mu M \end{array}$ 

Immunomodulatory Activity Oxidative Burst Inhibition (IC<sub>56</sub>µg/mL) WB 5.7  $\pm$  0.8 PMNs3.4  $\pm$  0.1 Ibuprofen (Standard) WB 11.2  $\pm$  1.9 PMNs 2.5  $\pm$  0.6

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#### VII.B-4

## Bergenin Loaded Xanthan Stabilized Silver Nanoparticle Prevents Arthritis by Suppressing Th1/Th2 Cytokines and TLR2/4 mRNA Expression in Adjuvant-Induced Arthritis Rats

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Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammation of joints associated with massive infiltration of activated immune cells and cartilage or bone destruction. Various plant-derived flavonoids and polyphenols found to be effective in controlling RA progression. Bergenin (BG) is a C-glucoside, hydrolysable tannin possesses various pharmacological activities, however, its stability and bioavailability are majorly compromised. The present study demonstrated the successful fabrication of gum xanthan stabilized silver nanoparticles with bergenin (GX-AgNPs-BG) characterized through UV-vis, zetasizer, FT-IR and AFM, which was further tested against CFA-induced arthritis model targeting ROS, cytokines & TLRs expression. Comparing to the pure compound (BG; 25mg/kg), oral administration of GX-AgNPs-BG (1mg/kg) exhibited potent anti-arthritic activity with minimal arthritic score, mild to moderate paw tissue swelling, reduced degenerative changes along with mild articular changes and lesser influx of inflammatory cells in macroscopic, X-Ray and histological examination, respectively. The treatment of BG and GX-AgNPs-BG significantly suppressed the levels of reactive oxygen species (ROS) including nitric oxide (NO) and hydrogen peroxide (PO) compared to the arthritic control group. Moreover, increased production of O2<sup>•-</sup> in human neutrophils, stimulated by opsonized zymosan (OZ) and phorbol-12-myristate-13-acetate (PMA) were also suppressed. Thereby, revealing the ability of BG and GX-AgNPs-BG to antagonize the oxidative stress via interference with NADPH oxidase metabolic pathway. Toll-like receptors (TLRs) is a pattern recognition receptor that bridges innate and adaptive immune systems and participate in arthritis development. In this study BG exhibited its anti-arthritic effect suppressing the TLRs (TRL-2 & -4) expressions. Additionally, the cytokine network regulates a broad range of inflammatory processes that have been implicated in the pathogenesis of RA and the balance of Th1/Th2 cytokines is thought to influence the autoimmune disease. BG and its nanoparticle inhibited the pro-inflammatory cytokines (IL-1 $\beta$ , IL-6 and TNF- $\alpha$ ) production with the induction of anti-inflammatory cytokines including TGF-β1 and IL-10 and IL-4 in spleenocytes. Taken together, the current investigation validated that GX encapsulated AgNPs as stable nano-cargo for embattled delivery of BG with improved stability, enhanced efficacy, increased solubility and targeted delivery meets the criteria for drug formulation and might be a new promising multi-targeted therapeutic strategy for RA treatment.

## **Session VIII.A**

## **Proteomics and Metabolomics II**

Chair: Lorenza Putignani I.R.C.C.S. 'Bambino Gesù', Italy

### VIII.A-1 - Key-Note Lecture

### A Proteomic Perspective of the Role of Oligogalacturonides in Plant Defence and Development

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Plants are challenged by a wide range of biotic stresses like fungal, bacterial, or viral infections. Pesticides remain largely used to prevent crops from diseases but their high cost and secondary effects on the environment, human health, and selection of resistant strains stimulate research of new strategies for a more sustainable crop production. Elicitor-induced resistance against pathogens is a strategy of crop protection under investigation, and carbohydrate elicitors are presently studied and experimented for their possible role as resistance inducers.

Oligogalacturonides (OGs), fragments derived from the hydrolysis of plant cell wall homogalacturonan by fungal polygalacturonases, are well known damage-associated molecular patterns (DAMPs). In Arabidopsis thaliana, perception of OGs triggers an intracellular signaling cascade that initiates defence against pathogens. OGs may also work as regulators of plant growth and development mainly through their antagonism with auxin (IAA). However, most of the mechanism by which the OG signal is transduced is not yet known.

In this study, the signaling events specifically activated by OGs were investigated by quantitative proteomics and phosphoproteomics in membrane-enriched fractions and in nuclear extracts. The functional role of a plasma membrane associated protein (PCaP1) in elicitor-induced protection was studied by a reverse genetics approach. The nuclear proteome was analyzed in response to IAA, OGs or a IAA/OG co-treatment, to identify regulatory elements that mediate the OG/IAA antagonism. The observed changes may arise not only from altered expression but also from post-translational modifications, degradation and/or translocation of proteins to different compartments. Interesting candidates in OG/IAA antagonism have been identified and their functional role is under study.

### VIII.A-2

# *In Vivo* Phosphoproteomics Reveals Pathogenic Signaling Changes in Diabetic Islets

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Progressive decline of pancreatic beta cells function is key to the pathogenesis of type 2 diabetes. Protein phosphorylation is the central mechanism controlling glucosestimulated insulin secretion in beta cells. However, if and how signaling networks are remodeled in diabetic islets *in vivo* remain unknowns. Here we applied high-sensitivity mass spectrometry- based proteomics and quantified the levels of about 6,500 proteins and 13,000 phosphopeptides in islets of obese diabetic mice and matched controls. This highlighted drastic remodeling of key kinase hubs and signaling pathways. We integrated our phosphoproteomic dataset with a literature-derived signaling network, which revealed a crucial and conserved role of GSK3 kinase in the control of the beta cells-specific transcription factor PDX1 and insulin secretion, which we functionally verified. Our resource will enable the community to investigate potential mechanisms and drug targets in type 2 diabetes.
#### VIII.A-3

## Metabolite Profiling of β-Thalassemia Patients Treated with Hydroxyurea

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 $\beta$ -Thalassemia is one of the most prevalent forms of congenital blood disorders characterized by reduced hemoglobin levels with severe complications, affecting all dimensions of life. Current standard treatment of  $\beta$ -thalassemia is based on symptoms of each patient. Augmentation of fetal hemoglobin (HbF) production has been an enduring therapeutic objective in  $\beta$ -thalassemia patients for which hydroxyurea (HU) have largely been the drug of choice and the most cost-effective approach.

Advancements in metabolomics offer an efficient solution to study the complexity of diseases at the molecular level that expands treatment strategies. This study is designed on metabolite profiling to improve mechanistic understanding of phenotypic heterogeneity of  $\beta$ -thalassemia and hence better management of this disorder. Firstly, untargeted serum metabolites were analyzed after protein precipitation and SPE (solid phase extraction) using gas chromatography-mass spectrometry (GC-MS). Then, a follow up metabolomics study on the serum of  $\beta$ -thalassemia patients before and after HU administration was done The HU treated patients were further classified into good (GR), partial (PR) and non-responders (NR) according to their response. 25 metabolites that were altered before HU therapy at p ≤0.05 and fold change >2.0 in  $\beta$ -thalassemia patients; started reverting towards healthy after HU treatment.

Metabolic pathway analysis also revealed that metabolism of linoleic acid, glycerolipid, glycerophospholipid, galactose, fatty acid biosynthesis, metabolism and their elongation in mitochondria were also reverted after HU therapy. Then targeted quantification of free fatty acids (FFAs) was carried out to disclose the prognosis of HU in  $\beta$ -thalassemia using the combination of random forest (RF) with gas chromatography-multiple reaction monitoring-mass spectrometry (GC-MRM-MS). Moreover, effect of HU therapy on apolipoprotein A1 and B protein was analyzed by ELISA. In inference, we noticed that HU therapy not only reduces need of blood transfusion in  $\beta$ -thalassemia but also corrects the serum FFAs profile and lowered the apolipoproteins ratio (apo B/apo A1), thus reducing the risk of CVD in these patients. Details will be discussed in the lecture.

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## September 7<sup>th</sup>

## **Session VIII.B**

## Agrifood

Chair: Luciana Dini Sapienza University of Rome, Italy

## Nanotechnologies and Strategies for the Active Containment of *Xylella* fastidiosa in Puglia: "In Planta" Experiments

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The olive trees quick desiccation syndrome, is the disease of olive trees observed in Salento (Puglia, southern Italy) associated with Xylella Fastidiosa infection (X.f.) [1,2]. The impact of infection from X.f. it is devastating for the local economy, especially considering the high value of ancient monumental olive trees (trees over the age of 100). Although the traditional approach to bacterial diseases is the eradication of infected plants, the economic value of each tree requires the experimentation of alternative strategies.

Our approach is based on the development of nanocarriers made with non-toxic, biocompatible and extremely economical materials in order to obtain an economically and environmentally sustainable solution.

Preliminary studies conducted in our laboratory have demonstrated the mobility of nanovectors in xylematic vessels, with no effect on plant tissues and damages due to absorption by plant cells. The mobility of the nanoparticles was observed in sections of xylematic vessels using a confocal microscope.

The nanocarriers are therefore free to travel and a selectivity towards the bacteria was also boserved. The release of specific anti-Xylella substances is now object of our studies.

Given the encouraging results obtained in the laboratory, the "in planta" experiments were started, aiming to demonstrate the effectiveness of the nanopreparate and optimizing the conditions for the forthcoming field trials.

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## Development of Nanocarriers from Lignocellulosic Wastes forFood Packaging and Nano-Biopesticides

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Biomass represents a source of active molecules with multiple potential applications in the agri-food sector, including plant protection. Through micro-and nano-technological approaches it is possible to develop eco-sustainable and efficient systems for the management of plant-borne diseases, allowing the assembly and release of specific natural active ingredients. In this context, the goal is to highlight how the use of lignocellulosics, through nanotechnological approaches, can replace the use of chemical and green pesticides. At the same time, new sustainable, antimicrobial and antioxidant systems, even at the nanoscale, have been rapidly promoted in the food packaging sector as a viable eco-compatible solution to improve the safety and quality of food products, to reduce environmental impact of traditional materials and, above all, to contrast in an eco-sustainable way, different microorganisms (bacteria and fungi) agents of huge economic losses. An overview of the current nanotechnological strategies is presented, valorizing biomasses of different origins involved in the protection of food and plants, taking into account the use of sustainable substances instead of chemical molecules. The lignocellulosic biomass, obtained from various natural sources of agro-forest industrial residues, are considered due to their natural antioxidant and antimicrobial activities, combined with natural active ingredients for the development of new reinforcement phases for traditional and/or biodegradable polymer matrices in active packaging systems and for nano-biopesticides. Cellulose nanocrystals and/or different micro- and nano-particles, linked to natural substances, are considered for packaging of fresh consumption agro-food productions, as for eco-sustainable phytoiatric formulations.

## Characterization and Properties of Some Seed Coating Formulations Based on Natural Polymers

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Although recently introduced, film-coating of agronomic seeds is now widely accepted in modern agriculture as an effective technology for protecting germinating seeds and seedlings<sup>1</sup>. Seed treatments can be useful in reducing the amounts of pesticides required to manage a disease and to enhance the growing of plants<sup>2,3</sup>, because the lack of water and desertification are extreme problems for plant survival and growth in the arid and semiarid areas of the world.

This work was done to provide information about possible film-forming polymers which can be used as suitable candidates for seed treatment formulations and to find out which properties are important for a good coating. Polymers used in this work were kcarrageenan reinforced with cellulose nanocrystals (CNC) or bentonite (BT).

Structural evaluation of films which can be used as seed coating was done by FT-IR spectrometry and X-ray diffraction, and the morphological aspects by AFM and TG measurements. For further characterization, were performed sorption measurements at different relative humidity, water sorption capacity being evaluated through the gravimetric method and near infrared spectroscopy. The hygroscopicity was observed by doing the moisture pick-up test, dry-in time of water droplets on the surfaces and contact angle measurements, this property being important since high water-uptake can result in agglomeration of the coated seeds. It was observed that with increasing the content of reinforcing agent, the hygroscopicity of films decreased. In addition, the film forming solutions were applied on seeds and the impact of formulations on seeds was observed.

In conclusion, the seed coating formulations are a safer, cheaper and more environmentally friendly alternative, without causing any pollution and having significant economic and environmental benefits<sup>4</sup>.

**Acknowledgements:** This work was supported by a grant of the Romanian National Authority for Scientific Research and Innovation CCCDI-UEFISCDI, project number COFUND-M-ERA.NET II-COMPIO, within PNCDI III.

## Liquid-liquid Extractions and Chromatographic Profiling of Flavonoids in the Hydro-Alcoholic Extract of *Azadirachta indica* (Neem) Leaves

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Azadirachta indica, commonly known as neem, is a tropical and semi-tropical tree in the mahogany family Meliaceae originate from Pakistan, India and Thailand. Neem leaves contain several natural compounds, showing many biological activities, exploited to treat various diseases and disorders, including also cancer and HIV/AIDS. We had already demonstrated that in diabetic rats treated with the hydro-alcoholic extract of Azadirachta indica leaves, streptozotocin-induced intestinal ileal and pancreatic islet lesions were prevented, and the hepatic glycogenosis, pancreatic and liver oxidative status was ameliorated. Neem leaves are rich in flavonoids, that exhibit, besides the antidiabetic and antioxidant proprieties, also other important pharmacological activities targeting almost all organs in the human body. In order to produce a purified neem leaves extract particularly enriched in flavonoids, the ethanolic extract of Azadirachta indica leaves underwent further liquid-liquid extractions by using three different organic solvents, *i.e.*, dichloromethane, ethyl acetate and n-butanol, chosen among those commonly used for the preparation of food additives and flavouring agents in food and beverage industries. After three consecutive extractions, qualitative and quantitative analyses of samples were carried out by using Thin Layer Chromatography (TLC) and High Performance Liquid Chromatography (HPLC). Kaempferol-3-O-β-D-glucoside (C<sub>21</sub>H<sub>20</sub>O<sub>11</sub>, astragalin), kaempferol-3-O-rutinoside (C<sub>27</sub>H<sub>30</sub>O<sub>15</sub>, nicotiflorin), quercetin-3- $O-\alpha$ -L-rhamnoside ( $C_{21}H_{20}O_{11}$ , quercitrin), quercetin-3- $O-\beta$ -D-glucoside ( $C_{21}H_{20}O_{12}$ , isoquercitrin) and quercetin-3-0-rutinoside (C<sub>27</sub>H<sub>30</sub>O<sub>16</sub>, rutin) were the most present flavonoids found. By comparing the HPLC chromatograms of purified extracts obtained with the different solvents it was found that the qualitative-quantitative composition of flavonoid is depending on the extraction solvent used; in particular, dichloromethane allows extraction of 89.5% quercitrin, 5.3% isoquercitrin, 5.2% rutin; ethyl acetate allows extraction of 4.1% astragalin, 6.7% nicotiflorin, 12.0% quercitrin, 50.3% isoquercitrin, 26.9% rutin; n-butanol allows extraction of 6.2% nicotiflorin, 6.0% isoquercitrin, 87.8% rutin. Thus, depending on the specific purposes and needs (drugs, food supplements, cosmetics and other products based on the purified neem leaves extract) each of these three extraction solvents has the potential to prepare the product enriched with the most suitable flavonoids.

## Purification and Characterization of Anti-inflammatory Protein from Solanum nigrum

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The Solanum nigrum (Black nightshade) belongs to the family of Solanaceae. An annual herbaceous plant is native to north western Africa, Europe and central Asia. The whole plant, rich in variety of chemical constituents, significantly apply for treatment of multiple diseases and found to be beneficial for human health from ancient times. In present study for the investigation of biological active proteins from Solanum nigrum, the 9 KDa protein with anti inflammatory activity was purified. The protein was isolated by ammonium sulfate precipitation then Sephadex G100 chromatography and finally purified by Reverse Phase HPLC. The electrophoresis (SDS-PAGE) profile showed protein bands of molecular mass of approximately 9 kDa and electrospray mass spectrometry (ESI-MS) revealed the exact mass of a 9.34 KDa. This purified protein showed anti-inflammatory activity and inhibited the carrageenan induced paw edema when injected intravenously. Further the effect of protein on Carrageenan-induced IL-1 $\beta$ , TNF- $\alpha$  and MCP-1 was measured in peritoneal leukocytes by RT-PCR. Result indicated that the oral administration of protein, 30 min before Carrageenan injection, clearly down regulated IL-1 $\beta$ , TNF- $\alpha$ , and MCP-1, mRNA expression compared with the control group.

# September 8<sup>th</sup>

## **Session IX.A**

## **C-based Materials**

Chair: Maria Letizia Terranova University of Rome Tor Vergata, Italy

**C-based Materials** 

#### IX.A-1

## Chemical Methodologies to Introduce SiV<sup>-</sup> and Si-Ni Color Centers in Conductive CVD-grown Diamond

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The need of a new-solid state multifunctional devices is triggering researchers to explore materials and strategies for the production of systems conductive and optically active at the same time. To this aim, diamond with inclusions demonstrated to be a promising candidate showing good electrical and optical properties. In particular, the photoluminescence from Si-V- center is gaining even more attention due to the ability to concentrate about the 70% of its light emission into the ZPL peaked at around 738 nm. The present contribution deals with the ability of Ni to promote the introduction of Si-Vand Si-Ni color centers into the diamond lattice during the Chemical Vapor Deposition (CVD) growth of polycrystalline films on Si substrates. Moreover, the incorporation of Ni makes diamond sample conductive. The suitable Ni precursors for the introduction of Si and Ni inclusions were found by performing a systematic study on experimental synthesis conditions. The Ni was deposited by both chemical and physical methods and the effect of Ni on the final features of the diamond systems was investigated as a function of substrate pretreatment, growth time, nickel film thickness, etc. PL measurements evidenced a multi-wavelength emission due to Si-V- and Si-Ni color centers. Depending on the Ni amount and the duration of the synthesis process, I-V measurements showed resistivity values between ~10<sup>3</sup> and ~10<sup>-4</sup>  $\Omega$ ·cm and Hall effect measurements disclosed carrier mobility values ranging from 5 to 160 cm<sup>2</sup>V<sup>-1</sup>s<sup>-1</sup>.

In the view, CVD techniques may be considered a successful methodology for a controllable production of conductive diamond samples characterized by more than one ZPL and applicable in many advanced opto-electronic technologies.

**C-based Materials** 

#### IX.A-2

### Chemical Bonding and Microstructure of Graphitic Contacts in Femtosecond Laser Irradiated Diamond

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Structural properties of 3D graphitic electrodes in crystalline diamond are investigated by Micro-Raman spectroscopy measurements performed in a confocal backscattering geometry with spectral and spatial resolution of 1 cm<sup>-1</sup> and 1  $\mu$ m, respectively. Electrode structure is formed by buried graphitic pillars connected by strips on the surface, both realized by femtosecond laser irradiation. Within treated area, spectra confirms that laser processing partially modifies the sp<sup>3</sup> bonding of diamond and promotes the formation of sp<sup>2</sup> carbon phases used as contacts for carrier collection in radiation detectors. In this study we focused our attention on sp<sup>2</sup> bonded carbon phases, giving their contribution as a *D* peak around 1350 cm<sup>-1</sup>, related to breathing modes of C rings, and a G band, involving the in-plane bond-stretching motion of C  $sp^2$  atoms (arranged either in linear chains or rings) around 1580 cm<sup>-1</sup>, which can extend up to 1630 cm<sup>-1</sup> for short, strong carbon-carbon double bonds (as it occurs in olefinic molecules). In the middle of surface strip contacts, spectra are mainly characterized by a symmetric, broad G-like band at about 1580 cm<sup>-1</sup>. Approaching the graphitic carbon/diamond interfaces, the symmetric graphitic band extends toward lower wavenumbers. Such a widening is related to the softening of the *G* peak, suggesting the occurrence of different degrees of bond length and bond angle disorder. The increased structural disorder is also reflected in the sp<sup>3</sup> tissue, where a widening of diamond peak is observed. On the pillar surface, the G-like band becomes asymmetric due to the appearance of a 1620 cm<sup>-1</sup> vibrational contribution, linked to C sp<sup>2</sup> double bonds, which could introduces structural stress able to remove the threefold degeneracy in crystalline diamond, thereby resulting in the locally observed diamond peak splitting.

Deconvolution of experimental data into different components reflecting the nature of carbon domains is used to identify the spectral signatures of optimized contacts for all carbon radiation and particle detectors.

#### IX.A-3

## A Multidisciplinary Approach to Investigate the Interaction of Nanomaterials with Living Organisms

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The unique physicochemical properties of carbon nanomaterials make them promising candidates forbiomedical and biotechnological applications. In particular, the distinctive optical and structuralcharacteristics of single-walled carbon nanotubes (SWCNTs) have inspired the development of biologicallyapplicable optical sensors and molecular delivery scaffolds. Several studies have largely focused onenabling cell uptake of SWCNTs by engineering their surfaces through non-covalent side-wallfunctionalizations. Non-covalent functionalization with a rich variety of biomolecules and polymers hasbeen shown to potentially increase SWCNTs solubility and membrane translocation while endowing thesenanostructures with enhanced biocompatibility. Most studies have focused on eukaryotic cells; however, the effect of SWCNT functionalization on transport across the thick cell wall of prokaryotes remainsunexplored. In this study, we present a multidisciplinary approach to investigate the interaction between SWCNTs decorated with charged protein wrappings.

**C-based Materials** 

#### IX.A-4

## Modelling the Partial Reduction of Graphene Oxide for Advanced Biomedical Applications

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Graphene oxide (GO) is a versatile precursor to develop next-generation materials suited for several applications such as energy conversion, ultrathin electronics, biotechnology and tissue engineering. The characteristic properties of GO such as limited electronic conductivity, optical absorption and biocompatibility can be tuned by controlling its reduction degree, density and relative population of the oxygencontaining functional groups on the surface. In this perspective, several reduction approaches have been developed, based on thermal annealing, chemical or light treatments and electrochemical methods [1,2,3]. In the present contribution, we focused on the partial reduction of GO as a versatile approach to finely control the interaction between GO and biomolecules. In this contest, an understanding of the reduction mechanisms of the different oxygen-containing functional groups on the surface represents a fundamental issue to be addressed. Computational modeling of the main transformations of the GO surface during the electrochemical reduction as well a theoretical analysis of the presence and fate under reduction of oxidized surface group involved in the rGO/biomaterial interaction will supply a rationale for the partial reduction process.

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## September 8th

## **Session IX.B**

## **Chemical Technologies for Life Science II**

Chair: Hina Siddiqui University of Karachi, Pakistan

## Tracking Proteins Inside Living Cells via Metal-NTA-based Fluorescence Probes

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Small molecule-based fluorescent probes have been extensively used for real-time imaging of cells and tracking of various cellular events with minimal perturbation on the cells.[1] The (histidine)6-Ni<sup>2+</sup>-nitrilotriacetate system (Ni<sup>2+</sup>-NTA) has been widely used for protein purification, were also extensively exploited to site-selectively label large libraries of existing hexahistidine-tagged proteins *via* conjugation with fluorophores. A number of NTA-based probes with fluorophores conjugated with mono-NTA or *di-, tri*- and *tetra*-NTA derivatives to either mimic the concept of FlAsH or overcome the weak binding natureof His6-tag with Ni<sup>2+</sup>-NTA have been made. However, such probes often suffer poor membrane permeability and could hardly enter the cells without help of a penetrating peptide owing to highly negative charges of these moieties.

We have designed and synthesized metal-NTA based fluorescent probes, [2,3] consisting of a metal-NTA moiety, a fluorophore and an arylazide. By conjugation of NTA with a coumarin derivative, BODIPY or fluorescein and arylazide, followed by coordination with metal ions, a family of probes with blue, red and green colors was yielded. The probes, driven by Ni<sup>2+</sup>-NTA, bind specifically to a His6-tag genetically fused to proteins, with significant fluorescence turn-on upon photoactivation of arylazides of the blue and green probes. The arylazide of the blue and green probes is indispensable not only for fluorescence turn-on, but also for strengthening the binding between the probes and a protein. Significantly, the probes can rapidly enter different type of live cells to selectively target intracellular proteins with genetically fused His6-tag. Using these probes, we visualized subcellular localization of a DNA repair protein, Xeroderma pigmentosum group A (XPA122) and SIRT 5, a protein belonging to Sirtuin 2 family, which are mainly enriched in the nucleus and the mitochondria respectively. Moreover, the probes can be further utilized to track endogenous metal binding proteins inside live cells owing to the formation of covalent bonds between the probes and targeted proteins upon photo-activation of the arylazide. Therefore, the probes are metaltunable, allowing high throughput analysis of metalloproteomes in live cells. Our strategy provides a new opportunity for multiple-channel tracking and labelling of large libraries of His6-tagged proteins as well as metalloproteomes in various prokaryotic and eukaryotic cells.

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### **Bioinspired Synthesis: Chemistry for Biology**

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Natural products and their biosynthetic designs are a great source of inspiration to synthesize and disocver novel biologically interesting small molecules.[1] However, the de novo synthesis of natural products remains a daunting and often impractical method to afford the desired numbers and amounts of complex small molecules for screening purposes. Also, employing a significant number of easily or commercially accessible synthetic chemical libraries in biological screenings had made only unimpressive returns. In this presentation, our endeavours to concisely build structurally diverse and natural product based molecular scaffolds that are amenable to compound collection synthesis, in particular, by means of annulation and cascade reactions [2] shall be presented. The synthetic designs based on some biosynthetic principles will also be discussed. How a small molecule embodying structural similarity to a natural product unravels modulation of a very different biological function [3] and presents immense opportunities in drug and probe discovery will also be part of the discussion.



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## The *In Vitro* and *In Vivo* Dialogue between Died and Viable Cells: Bystander Effects and Exploitable Consequences

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The Bystander Effect (BE) is an important biological phenomenon that refers to the induction of *biological* effects that leads to damages very similar to a direct insult in distant and not directly affected by a chemical/physical stress cells. This effect, well known in ionizing radiation treatment, relies on reactive signals secreted from exposed cells and transmitted via gap junction or culture medium. Besides radiation, chemicals can also induce BE. In this study a protein synthesis inhibitor, *i.e.* cycloheximide (CHX), CHX-induced apoptotic U937cells and untreated THP-1 cells were choosen to investigate the chemical-induced BE. The biological effects of apoptotic U937 cells culture medium, called Conditioned Medium (CM), on THP-1 cells was evaluated by morphological analysis and by 1D 1H and 2D J-resolved (JRES) NMR metabolomic analysis to characterize the molecules involved in apoptotic U937-induced BE. Further, the in vivo effect of CM was evaluated by investigating activated fibroblasts, endothelial cells, macrophages and mononuclear inflammatory cells colonizing the inoculum site of CM in rat calf muscles. In summary this study indicates that: 1) a time-dependent BE (induction of cell death) was in vitro induced by CM of CHX-treated U937 cells; 2) CM of CHX-treated U937 cells induces *in vitro* macrophagic differentiation of THP-1 cells; 3) CM has low amount of energetic molecules, such as  $\alpha$ - and  $\beta$ -glucose and glucogenic amino acids, and an increment of Krebs' cycle intermediates; 4) activated fibroblasts, endothelial cells, macrophages and mononuclear inflammatory cells are in vivo recruited. These data suggest that CHX exposed cells could cause BE through the release, during the apoptosis process, of soluble factors into the medium. The recruitment observed in in vivo experiments of immune cells potentially involved in cancer and inflammatory management needs to be further investigated.

## Activation of M2 Muscarinic Acetylcholine Receptors by Orthosteric and Dualsteric Agonists in Glioblastoma Cancer Stem Cells: Effects on Cell Proliferation and Drug Resistance

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The involvement of muscarinic receptors in cancer has been largely documented. While M3 muscarinic receptors results to promote tumor growth and progression, M2 subtype negatively modulates cell growth and survival in different tumor types. Our previous studies demonstrated that M2 orthosteric agonist Arecaidine Propargyl Ester (APE), arrested cell proliferation and induced apoptosis in glioblastoma cell lines and in glioblastoma cancer stem cells (GSC), an undifferentiated GB subpopulation characterized by high chemioresistance.

Studies on glioblastoma stable cell lines have demonstrated that low doses of M2 agonist APE were able to counteract the drug resistance for conventional drugs such as doxorubicin (Doxo) and Temozolomide, negatively modulating the drug efflux pump AGCG2. Similarly, in GSCs, the hybrid (orthosteric/allosteric) muscarinic agonist N-8-Iper inhibited cell growth in a dose dependent manner and also impaired cell survival at low doses. The inhibitory effects of the N-8-Iper appeared to be mediated by M2 receptor activation, since they were strongly reduced by co-administration of the selective M2 receptor antagonist methoctramine as well as upon M2 receptor silencing. The dualsteric agonist N8-Iper also decreased the expression of ABC drug efflux pumps (C1 and G2) both as transcript and as protein. Moreover the co-treatment of M2 agonists with low doses of Doxo (6.2 microM) significantly affected cell growth compared with the treatment with Doxo alone. Our data suggest that M2 receptor agonists, decreasing the drug efflux pumps expression, may impair the cancer stem cell chemoresistance, making the tumor cells more responsive to low doses of conventional drugs and reducing the side effects induced by chemotherapy.

September 8th

## **Session X.A**

## Chemical-physical Approaches for Detection and Characterization

Chair: Emanuela Tamburri University of Rome Tor Vergata, Italy

#### X.A-1 - Key-Note Lecture

### Design of Gold Hierarchically Ordered Crystals Architectures for Electrochemical Detection of Traces of Molecules

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Nowadays, noble metallic nanostructures with unique morphology are widely used as new sensors due to their fascinating properties. Among various shapes, dendritic nanostructures have attracted much attention because of their large surface-to-volume ratio, high sensitivity and special texture with sharp tips and nanoscale junctions. Several methods have been developed to fabricate those specific structures such as electrodeposition, seed-mediated growth or wet chemical method<sup>1</sup>. Among all these processes, the chemical route is mainly used due to its simplicity and low cost. However, this technique requires to create proper conditions by adjusting reaction conditions<sup>2</sup> such as solvent, reactant concentration, additives, temperature and pH. Indeed, the nanostructures growth process, their size, shape and distribution depend on all these key parameters. The present study deals with a novel approach for a controlled growth pattern-directed organisation of Au flower-like crystals (NFs) deposited onto stainless steel plates to achieve large-scale functional surfaces. The spectroscopic and the electrochemical activity of the hierarchically structured surfaces have been investigated as a function of the size, morphology and distribution of the hierarchical metallic crystals. The method consists in the deposition of a soft nanoporous template<sup>3</sup>, on which Au NFs are grown by seed-mediated method. After the preparation of the pre-patterned surfaces, the second step corresponds to the growth of metallic nanostructures inside the pores of the masks. The size and morphology of the Au NFs are controlled by a site-selective heterogeneous nucleation and growth process. The growth mechanism of the template-directed synthesis of Au crystals arrays has been investigated as function of the different physico-chemical parameters. The optical and electrochemical properties of Au NFs arrays were studied as a function of their morphology and organization<sup>3</sup>. Dendritic Au nanostructures have appeared as excellent Raman-active candidates due to the presence of very sharp tips of multi-branched Au nanoparticles that leads to a large local field enhancement and a good SERS sensitivity. In addition, these structures have also been used as electrochemical sensors to detect traces of organic molecules present in a solution. A correlation of the number of active sites on the surface and the current charge by both colorimetric method and cyclic voltammetry of gold structures have allowed a calibration of the system. Results show that this sensing platform is able to detect traces of molecules below ppb concentration. This device represents a first step for the fabrication of MEMs device that could ultimately be integrated in a lab-on-chip system. This facile and simple multistep approach is particularly attractive due to its environmentally gentle processing conditions and represents an open pathway to several technologically large-scale nanomaterials fabrication such as hierarchically ordered crystal architectures for sensor applications.

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#### X.A-2

## From Nature to Molecular-Diagnosis: Design of Bio-Based Photoacoustic Nanoprobes

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Photoacoustic Imaging (PAI) is an exciting new modality that uses non-ionizing radiation for real-time imaging with high spatial resolution and penetration depth. A broad range of application areas for molecular PAI have been identified, including oncology, neuroscience and cardiovascular diseases; so far basic research studies and preliminary clinical trials have focused primarily on detection, staging and therapeutic monitoring in cancer. The development of bio-inspired NIR responsive nanomaterials plays a key role in improving sensitivity and signal-to-noise ratio in photoacoustic imaging. To date, a promising approach relies on the green synthesis of nanoparticles starting from natural or endogenous materials as a source of contrast.[1] Among those, eumelanins, hydrophobic natural pigments, are emerging as a powerful organic component for developing biologically active materials of their numerous biological functions, such as photo-protection. because photosensitization, free radical quenching, metal ion chelation and even intrinsic antimicrobial behavior. They combine safety with marked antioxidant features [2] as well as a broad band of absorption in the visible and near infrared (NIR) regions and thus can be potentially applied in Photoacoustic Imaging.

To date, several melanin- based probes have been reported with specific properties for PAI, however, poor solubility of eumelanins in biological fluids as well as poor contrast of PA signal, if compared to other contrast agents must be addressed. Solubility issues are usually addressed by conjugation of the biopolymer onto a foreign matrix, made of either organic or inorganic materials [3]. Among those, silica stands as an outstanding, safe and biocompatible choice to ensure chromophore stability as well as an improvement of PA signal amplitude, through confinement effect. Furthermore, Silica allows easy functionalization to guarantee active targeting, as well as long circulation times.

Following a bioinspired approach, we designed a prototype of PA eumelanin-based hybrid nanoprobe constructed by Redox interaction of eumelanin silica hybrid nanoparticles with Ag<sup>+</sup> ions. These nanoplatforms proved high stability towards aggregation and high biocompatibility and PA contrast enhancement.

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#### X.A-3

## Characterization of Nanostructured Calcium Carbonate Found in Ancient Etruscan Tombs

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In this work we have analysed a white substance, covering walls and paintings of two Etruscan tombs: *the Tomba degli Scudi* and *the Tomba Bartoccini*, located in the Monterozzi necropolis of Tarquina. In *the Tomba degli Scudi* this white patina is still in place and covers the frescoes. Before the intervention of restorers, we have investigated this deposition and through SEM\EDX, FT-IR and XRD analysis, discovering a particular nanostructured form of Calcium Carbonate, composed of nanorods, several microns long and with a thickness of 400 nm. Embedded in this white patina, the analysis of the microbial community has revealed the presence of actinobacteria, which, together with particular environmental conditions, could have a leading role in the formation of this kind of calcite. In particular, we selected bacterial strains able to depose (*Bacillus* and *Streptomyces* species) or to dissolve Calcium Carbonate in laboratory conditions. These results support the notion that microorganisms contribute to calcium carbonate deposition and this capability has a biotechnology application in the field of artwork restoration. The role of frescoes protection by this particular calcium carbonate deposition will be also discussed.

#### X.A-4

## Synthesis of Polynorbornene Dicarboximides Bearing Trifluoromethyl Isomer Moieties. Study of gas Transport Properties

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This work reports the synthesis and ring-opening metathesis polymerization (ROMP) of new structural isomers based on norbornene dicarboximides bearing trifluoromethyl moieties, specifically *N*-2-trifluoromethylphenyl-*exo,endo*-norbornene-5,6-dicarboximide (**2a**), *N*-3-trifluoromethylphenyl-*exo,endo*-norbornene-5,6-dicarboximide (**2b**) and *N*-4-trifluoromethylphenyl-*exo,endo*-norbornene-5,6-dicarboximide (**2c**), using tricyclohexylphosphine[1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-

vlidene][benzvlidene] ruthenium dichloride **(I)**, bis(tricyclohexylphosphine) benzylidene ruthenium (IV) dichloride (II), and bis(tricyclohexylphosphine) pfluorophenylvinylidene ruthenium (II) dichloride (III). It was observed that the -CF<sub>3</sub> moiety attached at the ortho position of the aromatic ring increases thermal and mechanical properties of the polymer, whereas *meta* substitution has the opposite effect. A comparative study of gas transportation in membranes, based on these fluorinated polynorbornenes, showed that -CF<sub>3</sub> ortho substitution increases permeability of the polymer membrane as a consequence of the increase in both gas solubility and gas diffusion. In contrast, gas permeability coefficients of the metasubstituted polymer membrane are rather similar to those of that which is nonfluorinated; this can be attributed to a lower fractional free volume. The metasubstituted polymer membrane, besides showing the largest permselectivity coefficients of all the isomers studied here, was also found to have one of the largest permselectivity coefficients for separating  $H_2/C_3H_6$  into glassy polynorbornene dicarboximides.

## September 8th

## **Session X.B**

## **Material Chemistry & Technology**

Chair: Mauro Pasquali Sapienza University of Rome, Italy

## Synthesis and Characterization of Super Absorbent Polymer Composite by Using Nano-Clay

#### Baloch M.M., Memon M.A., Akhtar M.W.

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Combining inorganic nano-fillers in polymer matrix enhances its physical, chemical and mechanical properties. In current study attempts have been made to synthesize a superabsorbent polymer composite material by the graft copolymerization technique of acrylamide, acrylic acid and Nano-clay in aqueous solution. Some optimized parameters have been studied, such as the weight ratio of the Nano-clay, the effect of the initiator, the crosslinking agent, of the copolymer which influenced the absorptions of the superabsorbent.

Varying percentages of nano-clay ranging from 30, 32, 34, 36, 38 and 40 wt.% was added in polymer matrix. Specimens were then immersed in tap, de-ionized and saline water for the time period ranging from 2 hours to 24 hours. Specimen containing 36 wt.% nano-clay exhibited highest water absorbency *i.e.*, 183.33% after immersion in tap water for 2 hours. Specimens with increased content of nano-clay *i.e.*, 38 and 40 wt.% were found to be less absorbent of de-ionized and tap water, which could be due to an increased creation of physical and chemical cross-links in the matrix of polymer. Whereas, immersion of specimens in saline water exhibit insignificant absorbency. Similar trend was recorded after immersion of samples for a period of 4, 6 and 8 hours containing 36 wt.% of nano-clay. Results obtained from thermogravimetric (TGA) analysis showed that addition 38 wt.% of nano-clay improved thermal stability of polyacrylamide matrix up to 350 °C.

## Enhancement of Mechanical Properties of Short Bamboo Fiber Reinforced Composites with Alkali Treatment

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In the present study, epoxy resins have been reinforced with physically modified (alkali treated) short bamboo fibers to develop bamboo fiber-reinforced plastic (BFRP) composites. Short bamboo fibers have been treated with 5% solution of NaOH for 2 hours at room temperature. Composite samples have been synthesized by reinforcing untreated and treated short bamboo fibers in epoxy resin using hand layup method. The castings were put under load for 24 hours for proper curing at room temperature. Different composite samples have been synthesized by varying the fiber loading (10wt%, 20wt%, and 30wt% and 40wt%) under the categories of untreated and treated composites. Samples are then put to analysis and testing of mechanical properties like: tensile strength, flexural strength, and hardness and impact strength. A comparative analysis shows that the optimum results have been obtained at 40% fiber loading. Alkali treatment has also improved the mechanical properties of composites. The morphology analysis reveals that the bamboo treated with 5% NaOH exhibited better compatibility with the epoxy and polyester resins than the untreated bamboo. The improvements in tensile strength and flexural strength were higher by 60% and 45%, respectively for 40% fiber loading composites with epoxy matrix. In the case of alkali- treated composites with epoxy matrix, the tensile strength and flexural strength were higher by 69 and 50%, respectively for 40% fiber loading composites.

## 3D Printing of Nanocomposites: Polymeric Materials for Additive Manufacturing

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This communication reports the use of detonation nanodiamond (DND) and graphene platelets dispersed in Poly(Vinyl Alcohol) (PVA), Polycaprolactone (PCL), Polyaniline (PANI) matrices as novel inks for 3D printing of variously shaped objects using a layerby-layer Additive Manufacturing method. In parallel with the nanocomposites preparation, in our labs a proper 3D apparatus has been designed and assembled for the printing of such nanocomposites. The protocols for material design, formulation, and the shaping of hybrid polymer-based materials have been settled choosing PVA-DND inks as a model system to test the performances of the 3D apparatus. The main factors influencing the quality of the final printed objects will be discussed, to enlighten the importance of the matching between the chemical/physical properties of the materials to be extruded and the characteristics of the 3D printer.

Some selected polymer-based systems printed by the 3D techniques will be presented, along their Thermal, Electrical and Mechanical properties.

### Synthesis of LiFePO<sub>4</sub> for Li-ion Batteries: a Kilo-Lab Tale

Scaramuzzo F.A.,<sup>1</sup> Paoletti C.,<sup>2</sup> Galli S.,<sup>2</sup> Prosini P.P.,<sup>2</sup> Pasquali M.<sup>1</sup>

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LiFePO<sub>4</sub> is widely exploited for the fabrication of cathodes in Li-ion batteries, because it has good specific capacity, excellent cyclic performance and relatively low cost. [1] The synthetic route and the physical properties of the precursors (e.g. dimensions and morphology of the particles), deeply affect the electrochemical properties of the material: as a consequence, it is crucial to obtain a sustainable method which allows to maximize the capacity. An efficient synthetic procedure, already successfully performed on lab-scale, uses FePO<sub>4</sub> as a precursor and is based on the following reactions [2]:

$$\begin{aligned} \text{FeSO}_4 + \text{NaH}_2\text{PO}_4 + \frac{1}{2}\text{H}_2\text{O}_2 + \text{nH}_2\text{O} &\Rightarrow \text{FePO}_4 \cdot \text{nH}_2\text{O} &\downarrow + \text{NaHSO}_4 + \text{H}_2\text{O} \\ \\ \text{FePO}_4 \cdot \text{nH}_2\text{O} &(\text{s}) + \text{H}_3\text{PO}_4 &\Rightarrow \text{FePO}_4 \cdot 2\text{H}_2\text{O} + \text{H}_3\text{PO}_4 + (\text{n-2})\text{H}_2\text{O} \\ \\ \text{FePO}_4 \cdot 2\text{H}_2\text{O} &\Rightarrow \text{FePO}_4 + 2\text{H}_2\text{O} &\uparrow \\ \\ \text{FePO}_4 + \text{CH}_3\text{COOLi} + 1.75 \text{O}_2 &\Rightarrow \text{LiFePO}_4 + 2\text{CO}_2 &\uparrow + 1.5 \text{H}_2\text{O} &\uparrow \end{aligned}$$

Moving from this know-how, we designed a process aimed to synthesize kilos of LiFePO<sub>4</sub> and optimized the production obtaining a material with specific capacity up to 160 mAh  $g^{-1}$  in batteries (being 170 mAh  $g^{-1}$  its theoretical maximum value).

Besides the production of semi-industrial amount of materials, our purpose is to promote the technology transfer to small and medium-sized companies, acting as a *trait-d'union* between academia and business world.

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# **Poster Session**

## Poster List

**P.01)** Ahali Abadeh Z., Zeolite Nanoporous Materials Loaded with Curcumin as Anti-Cancer Drug Delivery Systems

**P.02)** Ahmadi-Zeidabadi M., Dual Action of Electromagnetic Fields: Concomitant Exposure to an Extremely Low-Frequency Electromagnetic Field and Cancer Medication Could Increase or Decrease Drugs Efficiency in Brain Cancer

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**P.05)** Ansari M.N.H., Synthesis and Structural Studies of the Orbitide [1-8-NaC]-Zanriorb A1

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**P.10)** Campos do Vale J.R., Intramolecular Photochemical [2+2] Cycloaddition of Allylic Acylsilanes

**P.11)** Cannizzaro A., Use of Elemental Analysis to Measure the Potential Toxicity of Two High Temperature Insulation Wools

**P.12)** Delise T., A Review of Thermochemical, Solar Driven, and Water Splitting Cycles for Hydrogen Production

P.13) Dimiza F., Mn(II) with the Non-Steroidal Anti-Inflammatory Drug Flufenamic Acid

P.14) Han C.R., Isoflavonoids from the Roots of Ficus auriculata Lour

**P.15)** Hassan M., Cadmium Accumulation and Tolerance in Mungbean [Vigna radiata (L.) Wilczek] Genotypes Under Hydroponic Conditions

**P.16)** Holmsted S., New Bioactive Compounds from Natural Feedstock - Protection and Reduction on Quinic Acid

**P.17)** Jaiswal Y., Synthesis of Diverse Phenanthridiene via Palldium(II) Catalyzed Cascade Formation of C-C/C-C/C-N Bonds from Nitriles and Iodo Arenes

**P.18)** Kakoulidou C., A Zinc(II) Complex of a Quinazoline Derivative: Synthesis, Structure, DNA- and Albumin-Binding Studies

**P.19)** Kim M., Surface Oxidation of Noble Metal Nanoparticles Via Various Oxidants for Organic Reactions

P.20) Koval Ya.I., Unusual Methyl-Methylene Tautomerism of Bridged Oxazoles

**P.21)** Kumar Y., Visible-Light-Mediated Remote -γ-C(sp3)-H Functionalization of Alkylimidates: Synthesis of 4-Iodo-3,4-Dihydropyrrole Derivatives

**P.22)** Martínez A., *Metathesis Reactions: An Alternative to Prepare Biodegradable Unsaturated Linear Polyesters* 

**P.23)** Melchior A., Adsorption of Ciprofloxacin on Carbon Nanotubes: a Molecular Dynamics Study

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**P.25)** Osmanov H.M., The Level of Calprotectin and Main Parameters of Calcium-Phosphorus Metabolism in Osteoporosis Caused by Rheumatoid Arthritis

**P.26)** Osmanov H.M., The Study of Chemical Components of Cephalaria procera from Azerbaijan Flora

**P.27)** Ozturk I.I., New Binuclear Bismuth (III) Complexes of 5-Ethoxy-2-Mercaptobenzimidazole: Syntesis, Characterization and Cytoxic Activity

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#### P.01

## Zeolite Nanoporous Materials Loaded with Curcumin as Anti-Cancer Drug Delivery Systems

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In this work, a combination of different techniques has been used to assess the potential use of zeolite nanoporous materials for the delivery of natural bioactive curcumin. Curcumin is a water-insoluble drug extracted from turmeric (Curcuma longa) plant. In recent years, the potential anticancer effect of curcumin in suppressing many types of cancers, while showing a synergistic antitumor effect with other anticancer agents, has attracted great attention. However, the poorly soluble formulation of curcumin is a problem, which is normally overcome by the application of high drug dosage in oral formulations. Encapsulation of curcumin into a suitable carrier can render the drug completely dispersible and overcome its insolubility. Zeolites are inorganic crystalline aluminosilicates with porous structure on the nano- and micro-scale and high internal surface areas, which are known as adsorbents, molecular sieves and ion exchange materials. These properties of zeolites make them useful as pharmaceutical carrier systems to encapsulate drugs whit intrinsic low aqueous solubility and improve their dissolution. In our research, we explore the use of three different types of zeolites, X, Y, and A with different chemical composition and pore diameter, loaded with curcumin. The surface properties and morphology of these zeolite-based carriers, as well as the effect of drug loading and release, were investigated by means of scanning electron microscopy (SEM), powder X-ray diffraction (XRD), differential scanning calorimetry (DSC), and chemical analyses. Results regarding the release studies of the bioactive molecule from the different zeolites and the optimum conditions for drug loading will be reported. These results will indicate the potential of our zeolite carrier systems for curcumin loading and delivery in anti-cancer applications.

#### *P.02*

## Dual action of Electromagnetic Fields: Concomitant Exposure to an Extremely Low-Frequency Electromagnetic Field and Cancer Medication Could Increase or Decrease Drugs Efficiency in Brain Cancer

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Glioblastoma multiforme (GBM) is the most malignant brain cancer that causes high mortality in humans. It responds poorly to the most common cancer treatments, such as surgery, chemo- and radiation therapy. Temozolomide and Carboplatinis are an alkylating agent that has been widely used to treat GBM; resistance to these drugs is often found. One unexplored possibility for overcoming this resistance is a treatment based on concomitant exposure to electromagnetic fields (EMF) and drugs. Indeed, many evidences show that EMF affects cancer cells and drug performance.

In this study, we evaluated the effects of EMF alone and in combination with two drugs on human glioma cells lineU87 by the expression of P53, Bax, Caspase-3, Bcl-2, Cyclin-D1, heme oxygenase-1 (HO-1), MGMT( a drug resistance gene) GFAP (a differentiation gene) and reactive oxygen species (ROS) production.

The data suggest that the proliferation and apoptosis of human GBM are influenced by exposure to ELF-PEMFs in different time-dependent frequencies and intensities. And in combination method(EMF+ drugs) the results were very interesting. EMF increased the TMZ toxicity but reduced the effectiveness of Carboplatin.

The fact that some of the EMF frequencies and intensity favor cancer cells proliferation indicates precaution for the use of medical devices related to the MFs on cancer patients. On the other hand, some other EMFs Frequencies and intensities arresting cancer cells growth could open the way to develop novel therapeutics. In addition to combination therapy (electromagnetic and chemotherapy) could open a new field for develop more effective Strategy for cancer therapy in future.
# Phytochemical Investigation of the Roots of *Euphorbia bupleuroides* and Biological Activities

#### Aichour S.,<sup>1</sup> Lavaud C.,<sup>2</sup> Benkhaled M.,<sup>1</sup> Harakat D.,<sup>2</sup> Kassah-Laouar A.,<sup>2</sup> Haba H.<sup>1</sup>

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*Euphorbia bupleuroides* Desf. (*Euphorbiaceae*), a plant endemic to Algeria, has not been investigated previously. The CH<sub>2</sub>Cl<sub>2</sub> extract of the roots of *Euphorbia bupleuroides* vielded three new compounds with tigliane and triterpenoides: 4, 20dideoxy( $4\alpha$ )phorbol 12-benzoate 13- isobutyrate (**1**), 3 $\beta$ - hydroxy- cycloart- 25hyperoxide (2) and 3β- hydroxy- cycloart-25-ene-8,9-epoxid (3), respectively, to gather scopolétin (4), with nine known compounds: coumarinolignans(**5**). 24methylenecycloartanol (6), cycloart-23-Z-ene-3β,25-diol (7), 3β-hydroxycycloart-25ene-24-hydroperoxide (8), cycloartenol (9), cycloart-3 $\beta$ ,24,25-triol (10),  $\beta$ -sitosterol (11) and Daucostérol (12). Their structures were determined by combination of 1D and 2D NMR (COSY, HMBC, HSQC and NOESY) and mass spectrometry EI-MS and ESI-MS. The dichloromethane extract exhibited a moderate antibacterial activity against Staphylococcus aureus and Escherichia coli.

# Facile Synthesis of Hydrogel-Nickel Nanoparticle Composites and Their Applications in Adsorption and Catalysis

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Homopolymer bulk hydrogel of methacrylic acid with high degree of carboxylic groups were synthesized through a new single step facile rout and was used as template for the fabrication of nickel (Ni) nanoparticles. The prepared bare and composite hydrogel was characterized by Fourier transformation infrared (FT-IR) spectroscopy, Transmission electron microscopy (TEM), Electron dispersive spectroscopy (EDS), Thermal gravimetric analyzer (TGA), and X-Ray diffraction (XRD) technique. The carboxylic groups acted as highly efficient adsorption sites and their high degree was responsible for the removal of huge amounts of methylene blue and Rhodamine 6G from water. The maximum adsorption capacity of p(MAAc) hydrogel was 685 mg/g for MB and 1571 mg/g for Rh 6G. The adsorption data of MB was best fitted with Langmuir adsorption isotherm while that of Rh 6G with Temkin adsorption isotherm. It was found that the adsorption of both dyes was followed by pseudo second order kinetics. Catalytic property of p(MAAc)-Ni was evaluated by using it as a catalyst for the degradation of 4nitrophnol (4-NP) which is known as toxic pollutant. Effects of temperature, catalyst dose, and re-usability of catalyst on the reduction reaction were also studied. The apparent rate constant  $(k_{app})$  value of as maximum as 0.038 min<sup>-1</sup> was observed for the reduction of 4-NP while the activation energy (E<sub>a</sub>) for this reaction was 52 kJ/mol. It was found that this catalyst system can be used repetitively with a slight decrease in catalytic activity.

## Synthesis and Structural Studies of the Orbitide [1-8-N $\alpha$ C]-Zanriorb A1

Ansari M.N.H.,<sup>1</sup> Ganesan A.,<sup>2</sup> Jabeen A.,<sup>3</sup> Bashir A.,<sup>1</sup> Choudhary M.I.,<sup>1,3,4</sup> Shaheen F.<sup>1</sup>

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A new natural orbitide[1-8-N $\alpha$ C]-zanriorb A1(1) was identified from a folk medicinal plant *Zanthoxylum riedelianum* Engl. as a potent apoptotic agent against Jurkat leukemia T-cells (IC<sub>50</sub>= 218.0 nM). We performed solid-phase synthesis of **1** by two different routes. The route A involved the synthesis of a linear precursor **LP** of zanriorb A1 followed by solution phase cyclization of **LP** which afforded the inseparable rotamers (**W-8**) of zanriorb. Second route B involving complete synthesis of zanriorb A1 through on-resin macrocyclization approach, produced cyclic products **S-6** and **S-8**. The product **S-6** was also identified as an inseparable mixture of rotamers of natural product. While the minor product **S-8** was a different conformer of zanriorb A1. Interestingly, the second route also produced the unexpected hydrolysed linear precursor **S-2a** of **1**. For further confirmation, it was re-synthesized on solid phase which afforded **1a** having the same retention time and chemical data as **S-2a**. All peptides from the above studies were found to be inactive against Jurkat leukemia T-cells. However the linear precursor **S-2a** of zanriorb A1 inhibited nitric oxide (NO) (IC<sub>50</sub> = 88.1 ± 2.2 µM), produced from LPS activated J774.2 macrophagesas.

# Solid State Synthesis of CdTe Quantum Dots through Thermal Precursors Decomposition

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The synthesis of colloidal photo-luminescent semiconductor quantum dots (QDs), belonging to II-VI groups, even from single source precursors is presented. Since three decades their synthesis has been pursued implementing new and easier synthetic conditions that standardize their production. In this work is reported the production of luminescent of CdS QDs in a polymeric film induced by laser processing.

A film of PMMA doped with two types of precursors of cadmium carboxylate and tellurium phosphinate is deposited as a thin film to observe the formation of CdTe QDs.

The CdTe formation is observed after thermal annealing for different time by means of UV-Vis and photoluminescence spectroscopy.

The optical analysis showed the formation of CdTe QDs with size between 3–4 nm and with an emission photoluminescence included in the 540 650 nm region.

These results pave the way for patterning of QDs by inducing thermal annealing in selected areas of the film.

## Fungal-mediated Structural Transformation of Contraceptive Drugs, Drospirenone and Etonogestrel into New Metabolites

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Biotransformation is an efficient approach for structural alteration of all classes of organic compounds. This technique is effectively employed in green chemistry, particularly in drug discovery and development, as it involves a variety of enzymes during transformation which results regio-, chemo-, and stereo-selective products. In the current study, biotransformation of an orally active contraceptive drugs, drospirenone (1) and etonogestrel (7) was carried out at pH 7.0 and 26 ± 2 °C. Transformation of 1 with *Cunninghamella elegans* afforded four new metabolites, 14 $\alpha$ -hydroxy-drospirenone (2), 11-oxo-drospirenone (3), 12-oxo-drospirenone (4) and 11 $\beta$ ,14 $\alpha$ -dihydroxy-drospirenone (5), along with a known metabolite, 11 $\alpha$ -hydroxy-drospirenone (6) while transformation of 7 with *Cunninghamella blakesleeana* and *C. echinulata* yielded three new metabolites 6 $\beta$ -hydroxy-11,22-epoxy-etonogestrel (9), 10 $\beta$ -hydroxy-etonogestrel (10), along with two known metabolites 6 $\beta$ -hydroxy-etonogestrel (11), and 14 $\alpha$ -hydroxy-etonogestrel (12).



# Phytochemical Investigation of *Helianthemum hirtum ssp. ruficomum* (*Cistaceae*)

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*Helianthemum hirtum ssp. ruficomum* species belonging to the family *Cistaceae*, and including around 110 species of evergreen and semi-evergreen shrubs, the genus *Helianthemum* can be found in America, Europe and North Africa. However, the Mediterranean region is considered its center of diversity.

This work describes the isolation by chromatographic methods six flavonoid compounds from the aerial parts of AcOEt extract of plant H. *hirtum ssp. ruficomum*: Tiliroside (1), Astragalin (2), Isoquercétrin (3), Kaempférol 3-*O*-vicianoside (4), Quercétrin (5), Rutin (6). The structures of these compounds have been elucidated by means of spectroscopic studies including 1D and 2D-NMR and mass spectrometry ESI-MS, UV, measurement of optical rotation and by comparison with literature data.

# New Multitarget Cholinesterase Inhibitors with Metal-Chelating and Antioxidant Properties for Alzheimer's Disease

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Alzheimer's disease is a multifactorial degenerative syndrome, as many factors contribute to pathogenesis, among which the alterations of the cholinergic system, the overproduction and aggregation of the neurotoxic peptide  $A\beta_{42}$ , the oxidative stress, the dyshomeostasis of some metals that promote the aggregation of  $A\beta_{42}$  and catalyze the formation of ROS (1) (2).

Based on these considerations, a series of pyridine or pyrimidine compounds have been designed, synthesized and evaluated *in vitro*, with the hypothesis that they can inhibit cholinesterase and that they can have chelating and antioxidant activity, in order to obtain multitarget molecules for Alzheimer's therapy.

The compounds were designed based on the structure of cholinesterase enzymatic pocket, inserting two small aromatic groups separated by an aliphatic linker. In order to obtain compounds with metal-chelating activity, a 2-amino-pyridinic or 2-amino-pyrimidinic ring has been inserted as one of the two aromatic groups, while phenolic or catecholic rings have been introduced to confer antioxidant properties.

For the synthesized molecules, enzymatic kinetics studies were performed on *Ee*AChE and *eq*BChE, by Ellman's assay. Among the tested compounds the most potent inhibitor of *Ee*AChE showed a mixed-type inhibition mechanism with a Ki =  $0.312\pm0.108 \mu$ M, while the most potent inhibitor of *eq*BChE showed a mixed-type inhibition mechanism with a Ki =  $0.099\pm0.071 \mu$ M.

For the most potent molecules, the ability to chelate iron, copper and zinc ions was assessed through UV-vis spectrophotometry and antioxidant activity by means of the spectrophotometric method of DPPH.

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## Intramolecular Photochemical [2+2] Cycloaddition of Allylic Acylsilanes

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Acylsilanes have attracted great scientific interest<sup>1,2</sup> since their discovery in 1957 by Brook<sup>3</sup>. These compounds possess the unique ability to form reactive siloxycarbenes after photo-irradiation, which are able to perform metal-free OH-<sup>4</sup>, NH-<sup>5</sup>, CH-<sup>6</sup> and SiH-<sup>7</sup> insertion reactions. In addition, allylic acylsilanes are known to undergo intramolecular photochemical [2+2] cycloaddition of the carbonyl to the olefin. This method selectively yields oxasilabicyclo[2.2.0]hexanes in moderate to good yields.<sup>8</sup>

This study reports the preparation of a series of allylic acylsilanes substituted in the olefin moiety, synthetized through umpolung chemistry and metathesis. Replacing the olefin proton with an aromatic group results in a complete change in regioselectivity upon irradiation, leading to the [2+2] cycloaddition that exclusively yields the bicyclo[3.1.1]hexane regioisomer. These unstable compounds are readily converted to their more stable allylic alcohol structural isomers by treatment with catalytic amount of acid. The developed methodology provides a unique pathway for the synthesis of disubstituted silacyclopentenols.

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# Use of Elemental Analysis to Measure the Potential Toxicity of Two High Temperature Insulation Wools

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Biopersistence, fundamental parameter in the evaluation of fiber toxicity, can be determined carrying out in vitro dissolution tests by the measure of the dissolution constant (Kdis). Two wools belonging to high temperature insulation wools (HITW) were tested in saline solution: alkaline earth silicate wool (AES) and polycrystalline wool (PCW). The samples were kept at 37°C for 7, 14, 21 and 28 days at two pH values: pH 7.4 simulating interstitial lung fluids at and pH 4.5 to mimic the acid environment of alveolar macrophages. Size, morphological and chemical changes of fibers were studied by scanning electron microscopy (SEM-EDAX). Inductively coupled plasma atomic emission spectrometry analysis (ICP-AES) was used to measure the element concentrations of fiber released in solution during the dissolution process. Kdis is proportional to SiO<sub>2</sub> concentration released in solution for AES and to SiO<sub>2</sub> and Al2O<sub>3</sub> concentrations released in solution for PCW. The AES size distribution shifted to a larger mean diameter suggesting that there is a preferential loss of thin fibers. The respirable fibers decreased from 53% to 39%. AES wool showed a fast and extensive leaching of calcium after 28 days of treatment at pH 7.4 with a complete dissolution of fibers and formation of calcium phosphate precipitates on the fiber surface. The dissolution process of PCW led to transversal breakages of the fibers in both pH environments without involving chemical and morphological changes. The study showed that AES was more soluble than PCW at pH 7.4 as demonstrated by high value of Kdis (> 500 ng/cm<sup>2</sup>/h) comparing to PCW (79 ng/cm<sup>2</sup>/h). At pH 4.5, both wools broke transversely showing a similar dissolution behavior. Kdis is undoubtedly useful as a preliminary toxicologic screening of fibers, especially for developing fibers.

# A Review of Thermochemical, Solar Driven, and Water Splitting Cycles for Hydrogen Production

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The production of green fuels is a crucial issue for the preservation and improvement of the environment in large urban areas. The use of green fuels will allow to reduce the amount of carbon dioxide release in the atmosphere and hydrogen represents a totally ecological fuel for  $CO_2$  free power systems.

When Solar Power is employed, it is therefore necessary to develop efficient, economical, and sustainable hydrogen production methods to provide the necessary heat for water splitting. Three main routes can be identified: water electrolysis, biomass reforming, and thermochemical cycles.

All these methods haver widely been investigated over the past years and all of them show some promising feature.

The present work reports a state of the art survey of the different water splitting thermochemical processes (WSTP). These cycles can be classified in three different categories:

- Processes involving two chemical reactions, with one of the steps to be carried out at temperatures above 1000  $^{\circ}\text{C}.$ 

- Multiple steps processes, where the highest reaction temperature is below 1000  $^\circ\text{C}$ 

- Hybrid cycles that include an electrolysis step.

A in depth analysis, based on significant literature examples, of the advantages and disadvantages for the three configurations will be presented. The evaluation takes into account the different cycles overall performance considering also efficiencies and costs (where available) The results will be organised, summarised, and the three processes analysed will also be compared with other hydrogen production methods.

## Mn(II) with the Non-Steroidal Anti-Inflammatory Drug Flufenamic Acid

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Non-steroidal anti-inflammatory drugs (NSAIDs) comprise a group of medications used to treat inflammation, pain and fever. The main biological target of the NSAIDs is the inhibition of the cyclo-oxygenase (COX)-mediated production of prostaglandins [1]. The interaction of NSAIDs and their compounds with DNA (which is also a biological target of anticancer drugs) has been reported as a first approach to reveal their potential anti-inflammatory, antioxidant and anticancer activity [1,2]. Flufenamic acid (Hfluf) is an anthralinate NSAID [3].

Metal ions are important for many biological processes and are available in the human body and play essential role in cellular inspiration, signal transduction, memory storage and metabolism [4]. Manganese is among the most important biometals because of its presence in the active centre of many enzymes having diverse functions. According to literature reports, manganese compounds have exhibited promising anticancer, antimicrobial, antifungal and antioxidant activity [5]. The knowledge of metal activation of synthetic and natural drugs may be helpful for the development of more effective drugs and pharmaceutical formulations [4]. Metal complexes with NSAIDs have exhibited synergetic activity. Additionally, the presence of a nitrogen-donor heterocyclic ligand, such as 2,2'-bipyridine (bipy) or 1,10-phenanthroline (phen), increases the activity [1]. In this contribution, we present the synthesis, the structural characterization, the interaction with calf-thymus DNA and albumins as well as the antioxidant activity (scavenging activity of free radicals) of two novel neutral manganese(II) complexes with Hfluf in the presence of the nitrogen donor heterocyclic ligands bipy or phen.

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## Isoflavonoids from the Roots of Ficus auriculata Lour

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The *Ficus auriculata* lour belongs to *Ficus* genus of *Moraceae*. It has been used as Chinese folk medicine for the treatment of hyperactivity cough, nocturnal emission. The leaves of *F.auriculata* exhibited antioxidant, antiinflammatory, antidiabetic and hepatoprotective activities, and the fruits of *F. auriculata* exhibited significant antibacterial activity. [1-3] Previous chemical studies on this genus have led to the isolation of an array of compounds including triterpenoids, flavonoids, alkaloids and so on. [4-6] Six new isoflavonoids were isolated from the roots of *F. auriculata* (Fig. 1).



Fig. 1 The structure of compounds 1-4

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# Cadmium Accumulation and Tolerance in Mungbean [*Vigna radiata* (L.) Wilczek] Genotypes Under Hydroponic Conditions

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Cadmium (Cd) is the most hazardous metal naturally present in soil or anthropogenically released in agricultural fields. Screening of eight mungbean cultivars was performed that were obtained from National Agricultural Research Centre (NARC). Islamabad, Pakistan. Seeds were sown in plastic petri plates for 4 days in dark. Transferred into plastic tanks containing nutrient solution, allow growing for 10 days then provided with 0.1µM CdCl<sub>2</sub> in nutrient solution for 2 weeks at 26±2°C 16 h light and 8 h dark period with 70-80% humidity. Different morphological parameters were noticed. Cd concentration was analyzed by Inductively Coupled Plasma Mass Spectrophometry (ICP-MS). Xylem Sap was collected for 2 h to determined xylem flux and root-to-shoot translocation (Cd translocation). Our results showed decrease in all growth parameters in Cd treatment as compared to control. Significant difference in Cd concentration in xylem was noticed in treated plants among all genotypes that lead to the increment in Cd root-to-shoot translocation. Among all cultivars AZRI-2006 showed highest fresh weight of roots (FW r) and root retention (RR) capacity while NM-51 and NM 19-19 retained less Cd in roots so more Cd was translocated to shoots. Root retention capacity was significantly differ among genotypes in following hierarchal pattern NM 121-123>AZRI-2006>NM 2011>NM 13-1>NM 2006>NM 19-19>NM-51>NM 20-21. AZRI-2006 translocated less Cd in shoots, while NM 19-19 translocated more Cd so it can be used in excluding Cd at contaminated areas. AZRI-2006 was tolerant genotype as it was less affected by Cd treatment by exclusion procedure retaining more Cd in roots. NM-51 growth was severely affected by Cd treatment, so it found to be sensitive genotype. This research showed that hydroponics studies are the rapid method for screening of tolerant and sensitive genotypes of mungbean.

# New Bioactive Compounds from Natural Feedstock Protection and Reduction on Quinic Acid

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Finding new biomass-derived raw material is a possibility to go towards green chemistry by avoiding fossil resources, thus creating systems oriented by circular bioeconomy. By developing environmentally-friendly chemical processes, catalytic methods and atom economical pathways, we are able not only to reduce the carbon footprint but also create, for example, potential drug precursors.<sup>1</sup> Using biomass-derived compounds also allows to utilize cheap chiral molecules as starting materials.<sup>2</sup> Biomass-derived chiral molecules as starting materials of asymmetric synthesis responds to current financial, and most importantly, environmental demands when creating molecule libraries to biological assay use.

This study is based on quinic acid, a natural chiral polyol, which is a cheap material and easily modified due to its multiple functional groups<sup>3</sup>, namely four alcohol groups and one carboxylic acid moiety. Quinic acid was transformed into its lactone derivative and different protecting groups using the tridimensional arrangement of the vicinal diol framework were explored, allowing the preparation of six different lactone derivatives. Reduction of the lactone exposes a primary hydroxyl functionality that can be further explored due to its higher reactivity. By functionalization/defunctionalization of those alcohol groups, a library of different quinic acid derivatives was synthesized and is currently being studied in biological assays.

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# Synthesis of Diverse Phenanthridiene via Palldium(II) Catalyzed Cascade Formation of C-C/C-C/C-N Bonds from Nitriles and Iodo Arenes

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Palladium catalyzed C-H activation is widely accepted and efficient strategy for the synthesis of heterocyclic compounds. Phenanthridienes are important class of N-heteroaryl compounds having wide range of application in material science and serves as crucial building blocks for pharmaceuticals with potential therapeutic utility.<sup>1</sup> Apart for classical methods, a number of approaches have been developed including transition metal catalyzed reactions, metal free reactions and photochemical approaches.<sup>2</sup> In spite of these significant reports, a majority of the strategies relies on radical mediated chemical or photochemical reactions, which essentially requires pre-functionalized starting materials, therefore decreasing the step economy of the developed methods. There is no such single step protocol for direct synthesis of phenanthridiene from readily available starting material in literature.



Taking the recent reports into account and our research interests in metal catalyzed C-H activation,<sup>3</sup> we have designed a single step strategy for diverse synthesis of phenanthridiene via palladium catalyzed nucleophilic attack of aryliodie on arylnitrile followed by dual C-H activation. Convenient catalytic system, broad substrate scope, scalability and cascade formation of C-C/C-C/C-N bonds in single step makes this strategy efficient and attractive for organic chemist. Additionally, to support reaction mechanism, control experiments were performed, suggesting imine is crucial intermediate during the course of reaction.

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# A Zinc(II) Complex of a Quinazoline Derivative: Synthesis, Structure, DNA-and Albumin-Binding Studies

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Metal complexes with heterocyclic ligands have a great importance in medicinal chemistry. Quinazoline derivatives as *N*-heterocyclic compounds are frequently encountered in medicinal chemistry because of their therapeutical potency. In particular, quinazolines have exhibited various pharmacological activities such as antimicrobial [1], antimalarial [2], anti-inflammatory [3], anticancer [4]. In addition, they may act as EGFR inhibitor gefitinib 5 [5] and dual EGFR-ErbB2 inhibitor afatinib 64 [6].

Zinc is a trace metal essential for living organisms due its participating in many biological activities. Complexes of zinc with heterocyclic compounds have shown antitumor [7], anticonvulsant [8], antibacterial [9] and anti-inflammatory [10] activity. In this study, the synthesis and the characterization of a Zn(II) complex with a quinazoline derivative are presented as well as their interaction with calf-thymus DNA and serum albumins. The crystal structures have been determined by X-ray crystallography.

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## Surface Oxidation of Noble Metal Nanoparticles Via Various Oxidants for Organic Reactions

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Metal nanoparticles have been often used to heterogeneous catalysts for organic reactions. However, organic reactions via metal nanoparticles are limited because of neutral metal state (0) of nanoparticles. Thus, to broad scope of organic reactions, metal nanoparticles should have high valent oxidation state. Recently, Kim *et al.* reported surface activated Pd(IV) nanocatalyst for direct C-H halogenation and tandem cross-coupling reactions of benzo[h]quinoline. In this presentation, we report surface activation of noble metal nanoparticles via various oxidant such as N-bromosuccinimide (NBS), PhICl<sub>2</sub>, PhI(OAc)<sub>2</sub>. X-ray Photoelectron Spectroscopy (XPS) showed that activated metal nanoparticles have high valent oxidation states (Pd(IV), Rh(III)). Moreover, we analyzed coordination chemistry and oxidation state of nanocatalysts by using X-ray Absorption Fine Structure (XAFS).

## **Unusual Methyl-Methylene Tautomerism of Bridged Oxazoles**

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In this paper, a rare methyl methylene tautomerism has been investigated for bicyclic structures containing pyridinium and oxazolium cycles. These compounds were prepared according to the following strategy: allylation of various substituted pyridones and quinolinones with the formation of O and N isomers, halocyclization of the resulting compounds, followed by elimination. As a result, a structure containing an exomethylene function was obtained from 2-allyloxypyridine. In the case of N-allyl pyridone, an oxazolopyridinium compound was obtained. Reactions of these substances with various bases were also studied.

Oxazole derivatives have interesting tautomeric properties: their alkyl derivatives can exist as alkylidene tautomers. This type of methyl-methylene tautomerism is rather rare in the chemistry of azoles. We have studied a similar tautomerism for various bicyclic structures containing pyridinium and oxazolium cycles.

A scheme for the preparation of a d dihydroxazolopyrdine containing an exo-methylene function is shown below. This substance managed to convert to oxazolopyridinium only under harsh conditions by reacting with trifluoromethanesulfonic acid or boiling in perchloric acid. Under the action of bases, the opening of the oxazolium cycle occurs.



When applying a similar strategy to N-allyl pyridone, we immediately obtained an oxazolopyridinium compound.



A similar strategy has been applied to various substituted pyridones and quinolones.

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# Visible-Light-Mediated Remote -γ-C(sp<sup>3</sup>)-H Functionalization of Alkylimidates: Synthesis of 4-Iodo-3,4-Dihydropyrrole Derivatives

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Nitrogen-containing five membered heterocycles such as dihydropyrroles are one of the most important precursors in the organic synthesis. This class of compounds plays an important role in the pharmaceutical industry and broadly used as a versatile synthetic intermediate for the synthesis of various medicinally important products.<sup>1</sup> Consequently, several well-designed methods are available in literatures, a major issue lies with these reported protocols are: a) need of elaborated starting materials, b) requires a metal-catalyst or photo-catalyst (difficult to remove from the reaction mixture and eventually responsible for toxicity), and c) cost of the overall reactions. Pursuing these limitations, there is need to develop a convenient, efficient and cost effective strategy for the synthesis of functionalized dihydropyrroles, from readily available starting materials under mild reaction conditions.



With this understanding and our research interest to develop a new synthetic route for the synthesis of various functionalized organic molecules.<sup>2</sup> Herein, we are reporting an efficient and environmentally friendly synthetic approach toward functionalized dihydropyrrole derivatives. This developed protocol proceeds by the regioselective intramolecular C-N bond formation of alkylimidates *viz* 1,5-hydrogen atom transfer (HAT) of amidyl radical.<sup>3</sup> The major advantage of this designed strategy lies in choice of starting materials, mild reaction conditions, high regio and distereo-selectivity, clean source of energy and good functional group tolerance. Further, 4-iodo-3,4-dihydropyrroles could be easily transformed into a variety of useful derivatives. The stereochemistry of the products determined by NOESY analysis.

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# Metathesis Reactions: an Alternative to Prepare Biodegradable Unsaturated Linear Polyesters

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In the last two decades, there has been an interest in the use of biodegradable polymers as alternative to commodities plastics (CP); this concern has been driven by the increase of pollution. Biodegradable polymers can be originated from renewable and petrochemical sources. The most widely studied biodegradable polymers are polysaccharides and aliphatic polyester because they can achieve similar properties as the traditional CP.

In order to find an efficient synthesis route of polyester materials, the ring opening metathesis polymerization (**ROMP**) foreground from other due the control of physical and chemical properties. Nowadays, the **ROMP** challenge is the polymerization of non-strained macrocyclic monomers and those that possess functional groups able to deactivate the catalyst. This work shows the ROMP of  $\omega$ -hexadecenlactone and its copolymerization with norbornene, using ruthenium-alkylidene

[Ru(Cl)<sub>2</sub>(=CHPh)(PCy<sub>3</sub>)<sub>2</sub>] (I), [Ru(Cl<sub>2</sub>)(=CHPh)(1,3-*bis*(2,4,6-trimethylphenyl)-2imidazol-idinylidene)(PCy<sub>3</sub>)] (II) and the ruthenium-vinylidene [RuCl<sub>2</sub>(=C=CH(p-C<sub>6</sub>H<sub>4</sub>CF<sub>3</sub>))(PCy<sub>3</sub>)<sub>2</sub>] (III) catalysts. The high molecular weights between Mn = 109,00-114,800 g/mol and yields ranging from 94 to 98 % can be achieved by II catalysts. The catalysts II with the *N*-heterocyclic carbene ligand showed superior activity upon catalysts I and III bearing PCy<sub>3</sub> ligands. The percent crystallinity of the poly( $\omega$ -6hexadecenlactone) was 31 %.

## Adsorption of Ciprofloxacin on Carbon Nanotubes: a Molecular Dynamics Study

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The adsorption of neutral and zwitterionic form of ciprofloxacin (CFX), on single walled carbon nanotube (SWCNT) has been studied by molecular dynamics (MD) simulations. First, simulations in vacuum were carried out to investigate the interaction between inner and outer surface of SWCNT and 1, 2, 4, 8 CFX molecules. The CFX molecules remain close to the surface of the SWCNT and tend to aggregate through the formation of intermolecular hydrogen bonds. Similar results were obtained in water, however change in SWCNT-CFX morphology was observed after the solvent was added: CFX molecules interact with water by hydrogen bond leads to a dispersion of the molecules on the surface. The adsorption free energies ( $\Delta G_{ads}$ ) for zCFX and nCFX have been calculated both for the adsorption to the inner and outer surface of the SWCNT. All calculated  $\Delta G_{ads}$  values are negative highlighting that the process is thermodynamically favored with preference for the inner surface. The calculated  $\Delta G_{ads}$  for zCFX, which is the most abundant form in water at neutral pH appears to be in good agreement with the available experimental data.

# Unraveling Facet-Selective Electrodeposition Process of Cu onto Ag Nanocubes Via Single-Particle Plasmonic Imaging

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Fabrication of bimetallic nanomaterials by electrochemical methods have a variety of advantages in catalysis and sensing applications on account of their physical and chemical properties. However, obtaining electrochemically well-defined nanostructures in nanoscale-confined regions is not accessible. Herein, we exploited potential-controlled facet-selective overgrowth of Copper on energetically active surface of silver nanocubes through spectroelectrochemistry, including matlab-coded multi-particle imaging analysis. The experimental results show flower-like growth of Ag-Cu bimetallic nanostructures on (111) facet of Ag cubes as a function of applied potential, indicating Stranski-Krastanov mechanism. Changes of particle plasmon resonances during electrochemical surface reactions are correlated with results of FDTD simulations according to structural evolution, accounting for rationality on the kinetic and mechanism analysis. We explored the local distribution of electrochemical activities within a single nanocube, providing a great understanding on electrochemical bimetallic interconnection.

# The Level of Calprotectin and Main Parameters of Calcium-Phosphorus Metabolism in Osteoporosis Caused by Rheumatoid Arthritis

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Rheumatoid arthritis (RA) is the most common inflammatory joint disease, the prevalence of which is about 1%. Systemic negative effects on bone tissue in RA lead to the development of secondary osteoporosis (OP). The purpose of this research was to determine the level of calprotectin and parameters of the inflammatory activity of the disease - C-reactive protein, sialic acids, seroglucoids, antimicrobial peptide-defensin, calcium-phosphorus metabolism markers - calcium, phosphorus, magnesium, and also markers of bone metabolism - oxyproline, osteopontin, osteocalcin and the correlation between these parameters. Calprotectin, formed as a heterodimer of S100A8 and S100A9, is a member of the S100 calcium-binding protein family. It is expressed primarily by granulocytes and, to a lesser degree, by monocytes/macrophages and epithelial cells. In neutrophils, calprotectin comprises almost 60% of the total cytoplasmic protein content. Activation of the intestinal immune system leads to recruitment of cells from the innate immune system, including neutrophils. The neutrophils are then activated, which leads to release of cellular proteins, including calprotectin. The blood of 94 patients who were on hospital treatment at the Republican Arthrological Center was examined. All patients were divided into 3 groups. Group 1: RA patients with uncomplicated OP, group 2: RA patients with complicated OP, group 3 - RA patients with glucocorticoid (GC) - induced OP, which developed as a result of long-term steroid therapy. As a result, in all studied groups of patients a decrease in the level of calcium and magnesium was observed with the increase of the amount of phosphorus. It was revealed that the course of OP in RA is characterized by a decrease in osteocalcin by 38.0% and with an increase in the amount of free hydroxyproline and osteopontin by 26.8% and 44.4% respectively. In patients with RA with GC-induced OP, the level of osteocalcin was reduced by 49.9% with an increase in the content of free hydroxyproline by 44.5%. These data indicate a significant domination of resorption of bone tissue over bone formation. It was revealed that the level of osteopontin significantly increases in patients with OP having RA. In all groups, an increase in the level of calprotectin was observed by 41%, 47% and 23% respectively. Thus, in patients with RA early in the course of the disease, it is advisable to determine osteopontin, which can serve as an informative diagnostic marker for assessing the state of bone metabolism.

# The Study of Chemical Components of *Cephalaria procera* from Azerbaijan Flora

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Continuing the study of *Cephalaria* L. genus, fam. *Dipsacaceae* we have studied the chemical components of *C. prosera* Fisch. et Ave-Lalli [1,2].

*C. prosera* is used in folk medicine in the form of tea as a cardiotonic, patogonnoe, antipyretic and tonic [3].

We have studied the roots of *C. prosera* previously unexplored parts of the plant. The raw materials were harvested in early July 2014 in the vicinity of Khinalig, Guba region of Azerbaijan at a height of 2.5 km above sea level.

0.5 kg of raw material was extracted by ethanol in a ratio of 1: 8 (x2). The combined extracts were evaporated, added 150 ml of water, they were treated sequentially by hexane, chloroform and n-butanol. The substance **1** was obtained from the extraction of hexane, the substance **2** was obtained from the extraction of chloroform. The **5** substances (triterpenoid nature) were found from n-butanol extraction by separation method of TLC chromatography. n-Butanol was evaporated on a rotary evaporator, part of the extract was subjected to acid hydrolysis. The aglycones – a substance **3** and **4** were obtained from the resulting hydrolyzate by column = -p (eluents: chloroform, ethyl acetate).

Substance **1**: composition C29H500 m.p. 140-141°C (ethanol), -40° (with 0.6, chloroform). ReactionSalkovskogo and Lieberman-Burchard is positive.

Substance **2**: composition C30H48O3 mp 302-303°C (methanol) +79° (with 1.2, pyridine).

The substance **3** is identical with the substance **2** on the spectra identical dates.

Substance **4**: composition  $C_{30}H_{48}O_4$  mp 325-327°C (ethanol), +80° ± 2° (with 2.6, pyridine). Lieberman-Burchard reaction shows that the substances **2-4** are pentacyclic triterpenoids.

Based on the physico-chemical parameters of compounds substance **1** was identified as  $\beta$ -sitosterol, a substance **2** and **3** as oleanolic acid, a substance **4** as hederagenin.

Moreover, about 0.05% of sum of alkaloids were determined in the roots of *C. prosera*, consisting of four substances with Rf 0,80; 0.50; 0.29 and 0.13.

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# New Binuclear Bismuth(III) Complexes of 5-Ethoxy-2-Mercaptobenzimidazole: Syntesis, Characterization and Cytoxic Activity

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Bismuth (Bi) which is recognized as a low-toxicity metal in periodic table has been used in medicine since Middle Age. The major medicinal application of bismuth compounds are associated with various gastrointestinal disorders, ulcers and bacterial infections, such as caused by the pathogenic organism *Helicobacter pylori* [1]. The ligand and coordination geometry of complexes are believe to important forbiological activities of bismuth compounds [2]. Last studies demonstrated that bismuth complexes have sulfur containing ligands exhibit anticancer activities [3].

In this study, we notice the synthesis, characterization and biological properties of novel bismuth(III) halide complexes heterocyclic thioamide 5-ethoxy-2using mercaptobenzimidazole (EtMBZIM).  $\{[BiCl_2(\mu_2-Cl)(EtMBZIM)_2]_2.C\}$  $_{2}H_{5}OH$ (1),  $\{[BiBr_2(\mu_2-Br)(EtMBZIM)_2]2H_2O\}$  (2) and  $\{[BiI2(\mu_2-I)(EtMBZIM)_2]2\}$ (**3**) were synthesized from the reaction of bismuth(III) halides with 5-ethoxy-2mercaptobenzimidazole in 1:2 stoichiometry. Complexes 1-3 have been characterized by multiple spectroscopic techniques, thermal analysis, and single crystal X-ray diffraction (XRD) analysis. Complexes 1-3 were evaluated for their in vitro cytotoxic activity against human breast adenocarcinoma (MCF-7) and human cervix adenocarcinoma (HeLa) cell lines along with non-cancerous cells MRC-5 (normal human fetal lung fibroblast cells). They were also used to study their influence upon the catalytic peroxidation of linoleic acid by the enzyme lipoxygenase (LOX).

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# New Deferiprone Derivatives as Multi-Factorial Cholinesterase Inhibitors: Design, Synthesis and *InVitro* Evaluation

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A new series of deferiprone derivatives were designed, synthesized and evaluated as potential multifunctional cholinesterase inhibitors for Alzheimer's disease (AD). The investigations about these compounds have included the inhibition of acetylcholinsterase (AChE) from Electrophorus electricus and of butyrylcholinesterase (BChE) from equine, through Ellman's spectrophotometric method, the chelation studies of  $Zn^{2+}$ ,  $Cu^{2+}$  e Fe<sup>3+</sup> and the antioxidant activity evaluation. These compounds were designed as dual binding site AChE inhibitors: they have an arylalkylamine moiety, connected via an alkyl chain to a 3-hydroxy -4-pyridone fragment, to allow interaction with catalytic site of the enzyme (CAS) and peripheral anionic site (PAS). The most active compounds revealed acompetitve or mixed inhibition mechanism towards AchE and BChE, with Ki according to the order of low micromolar. The mixed inhibition mechanism might suggest an interaction with both CAS and PAS and a possible involvement in inhibition of  $A\beta$  plaques formation. Furthermore, these deferiprone derivatives are able to chelate Cu<sup>2+</sup> e Fe<sup>3+</sup>, indirectly attenuating oxidative stress. These experimental results were supported by a molecular docking study on human recombinant AChE (hrAChE). [1,2] Further studies are ongoing regarding their ability to inhibit the AChE-catalyzed aggregation of  $\beta$ -amyloid.

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# Analytical Method Development for Determination of Chitosan by LC-MS/MS and LC-RI for Dietary Supplement

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We have developed a sensitive and selective method for the quantitative assessment of the chitosan in related health functional food (dietary supplement). This method was developed by using a liquid chromatography-refractive index (LC-RI) and a liquid chromatographic-tandem mass spectrometry (LC-MS/MS). In this study, chitosan was hydrolyzed by acid hydrolysis into glucosamine whose concentration was determined by LC-RI and LC-MS/MS indirectly. The selective detection was performed by tandem mass spectrometry with electrospray source, operating in positive ionization mode and in multiple reaction acquisition (m/z 180  $\rightarrow$  162, 72, 84 for glucosamine). The standard calibration curves presented a linearity effect with the correlation coefficient  $(r^2) >$ 0.999 in both methods. The recovery results ranged between 89.3~102.9 % at 3 different concentration levels, and their relative standard deviations (RSDs) were less than 3.1% as noted in this study. This method makes it suitable for routine quantitative analysis of chitosan in both plain materials and dietary supplement formulations. We will argue that this research is evidence-based approach to assessment, thereby contributing to amendment of chitosan testing method for the Korean Health Functional Food Code.

## Au-Ag Hollow Nanocubes from Galvanic Replacement Reactions for Selective Electrocatalytic CO<sub>2</sub> Reduction

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Rising CO<sub>2</sub> concentrations in the atmosphere and the shortage on fossil fuels creates a demand for converting CO<sub>2</sub> molecules into useful products. Direct electrochemical CO<sub>2</sub> reduction is pointed out to be a viable solution for solving these demands. Especially, noble metal nanoparticles have been vastly applied to electrochemical CO<sub>2</sub> reduction for their highly selective nature in producing of CO. However, maximizing the active surface sites of nanocatalysts emerges as a main problem in the efficient utilization of noble metal nanoparticles. In this research, we have synthesized Au-Ag hollow nanocubes by applying galvanic replacement to Ag cubes. Ag cubes with an average size of 35 nm were first synthesized, and varied amounts of HAuCl<sub>4</sub> gold precursor were added to give hollow nanocubes from galvanic replacement reactions with different Au to Ag ratios. Through the integration of Au, the electrocatalytic properties including CO selectivity or overpotential were significantly enhanced from those of the template Ag nanocubes. Further analyses such as the effect of elemental composition variation are also discussed in relation to the enhanced electrocatalytic properties.

## Heterogeneous Pd(II) Salophen on Porous Polymer Catalysts for Heck Reactions

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Polymeric resins with large surface area were synthesized by suspension polymerization of commercial divinylbenzene (DVB) as cross linker, AIBN as initiator and different loading of o-phenylenediamine (AS=1, 2, 5, 10%wt) as co-monomer. The immobilization of Pd was further carried using Pd(OAc)<sub>2</sub> as precursor to be used as catalysts in C-C coupling reactions. The characterization was carried out by SEM microscopy, solid state UV-Vis, FT-IR (ATR), CP-MAS NMR, Raman, and ICP-OES. The ICP-OES indicate that eventhough it was immobilized a lower loading of Pd than the nominal, the fully characterization indicate a successfully immobilization of Pd maintaining the mesoporosity of the material. The catalysts were evaluated in two Heck C-C coupling reactions between iodobenzene (IB) as arvl halide, triethylamine as base and styrene or methyl acrylate as the alkene molecule in a carousel system using GC-MS Agilent model 5975C and a capillary HP-5m column. It was found that large surface area heterogeneous Pd catalysts were fully synthesis by a polymerization reaction using a porogen agent. It is noticeable the catalytic performance, similar to homogeneous Pd catalysts under similar reaction conditions with large selectivity and easy recovered at the end of the reaction.

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# Magnetic Pt Single and Double Core@shell Structures for the Catalytic Selective Hydrogenation of Cinnamaldehyde

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Magnetic single  $Fe_3O_4@SiO_2$  and double  $Fe_3O_4@SiO_2@TiO_2$  core-shell structures synthesized by successive coating steps from  $Fe_3O_4$ -NPs used as core followed by coating process with silica and titania alkoxide. The successfully synthesis was supported by a deeply characterization by means of SEM, EDX, HRTEM, DRX, FTIR and magnetic measurements. The finally deposition of Pt was carried out on the amine groups functionalized surface of the  $Fe_3O_4@SiO_2$  and  $Fe_3O_4@SiO_2@TiO_2$  core-shell structures contacting with 3-aminopropyl-triethoxysilane (APTS) in a reflux with toluene for 24 h to be used as catalysts in the selective hydrogenation of cinnamaldehyde (CIN) hydrogenation. The metallic clusters Pt-NPs show a narrow distribution and a mean particle size of ~3 nm. The catalytic activity performed in a batch Parr® type reactor at 100°C, 10 bar of H<sub>2</sub> using a substrate/catalyst (mol) ratio equal to 100 in a volume of 25 mL of cyclohexane, indicates for all catalysts a total CIN conversion before 4 h of reaction with the largest selectivity towards the hydrogenation of the C=O bond on the Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>@TiO<sub>2</sub> catalysts reduced at temperatures larger than 300°C.

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## Electrochemical Amidation of Alkylarylketones

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Amide function is very important in both organic and medicinal chemistry. Benzamides can be obtained in good to high yields by reaction of both deoxybenzoin and benzoin, primary or secondary amines, molecular oxygen and electrogenerated superoxide anion (obtained with galvanostatic method).

The advantage of using electrogenerated superoxide anion is related to its counterion, the tetraethylammonium cation, which is not tightly bound to the anion and thus renders superoxide highly reactive also in the absence of additives (necessary when using KO<sub>2</sub>). The reaction conditions are very mild and only 0.5 F/mol are necessary to obtain good yields in benzamides. This work points out that benzamides can be obtained starting from deoxybenzoin and benzoin, via C-C bond cleavage, with yields which depend on the charge amount.

Cyclic voltammetric analysis allowed to suggest a mechanistic hypothesis, which permits to explain the formation of byproducts and to define the role of oxygen and superoxide anion.

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Poster Session

#### P.34

## Dual Inhibitors of Urease and Carbonic Anhydrase-II from Iris Species

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Urease and carbonic anhydrase-II inhibitory activities of twenty seven known compounds 1-27, isolated from two species of *Iris*, were evaluated. Arborinone (1), alpinone (2), izalpinin (3),  $\beta$ -sitosterol (4), irisone A (5), betavulgarin (6), irisone B (7), irilin D (8), 5,7-dihydroxy-2',6-dimethoxyisoflavone (9), irilin B (10), tenuifone (11), irisoid A (12), and ethyl-β-D-glucopyranoside (13), were isolated from *Iris loczyi*, and (14), 5,7-dihydroxy-6-methoxychromone (15), 4',5,7-trihydroxy-6eupatorin methoxyflavanone (16), tectorigenin (17), kaempferol (18), apigenin (19), 4',5,7trihydroxy-3',8-dimethoxyflavanone (20), 8-methoxyeriodictyol (21), (E)-methyl-4hydroxy-3-methoxycinnamate (22), hispidulin (23), eupafolin (24), tectorigenin-4'glucoside (25), mangiferin (26), and 1,3-0-diferuloylsucrose (27) were obtained from Iris unguicularis. These compounds have been previously isolated from Irisloczyi and Iris *unguicularis*, except **8**, **14**, **19**, **22**, **27** and **25**, which were first time obtained from these plants. Their structures were deduced by comparing the data with reported spectral data. The urease and carbonic anhydrase-II inhibitory potential of these compounds were evaluated by using mechanism-based in vitro assays. Interestingly many of these compounds were found to be significantly active against both the enzymes. Compound **12** was the most active one in the urease inhibition assay with IC50 vaule of  $17.60 \pm 0.08$  $\mu$ M, while compound **3** was found to be most active against the carbonic anhydrase-II, having an IC<sub>50</sub> vaule of 66.27 ± 0.89 μM. Compounds **3**, **9**, **16**, **20**, **21**, and **26** were found to be dual inhibitors of both the enzymes.

## Phenolic Glycosides from the Stems of Homalium stenophyllum

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*Homalium stenophyllum* is a Chinese endemic plant, distributed in China's Hainan Island [1]. *H. paniculiflorum* have a range of biological activities such as antibacterial [2], antioxidant [2], antiviral [3-4]. Chemical investigation of the stems of *Homalium stenophyllum* led to the isolation and structural elucidation of two new phenolic glycosides, homastenoside H-I. The structures of the new compounds were elucidated on the basis of spectroscopic analyses including MS, 1D and 2D NMR data.



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## **Transfer of Chemical Elements from Milk to Dairy Products**

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The growing consumption of dairy products worldwide has stimulated in the last decade both the development of the production industry and the scientific research on the nutritional or toxicological properties of minerals and trace elements typical of dairy products. On the contrary, few researches have been directed to the analysis of chemical elements coming mainly from environmental contamination (e.g. lead, cadmium) or from manufacturing processes (e.g nickel, chromium).

The objective of this work was to evaluate the partition of As, Cd, Pb, Hg, Cr and Ni among the different dairy products. As the raw cow's milk contained low concentration values of these six elements of interest, it was spiked at concentration values such as to overcome analytical problems. In fact, the initial low content could have made less evident and/or not significant possible differences among different intermediate products (*i.e.* curd, whey, ricotta, primo sale and ripe cheese). Furthermore, the possible correlation between the behaviour of these elements and the behaviour of some components and macro-elements of milk was investigated as well.

Each product coming from cheese making was sampled and analysed for content of fat, dry matter, protein, macro and oligo-elements. Added elements were related to milk components both by studying concentration factors and statistical analysis.

Almost all elements considered, with the sole exception of As and Hg, seemed to shift preferentially into curds indicating a possible bond to certain proteins and fat component. As for Hg the link to fat could be only assumed taking into account their similar concentration factor in the intermediate and final products. Bivalent positive ions (Cd, Pb, Ni and Cr) could be complexed to casein through its phosphate groups that are negatively charged. It could be also assumed a similar association with low molecular weight ligand as citrate but the first hypothesis can be the most explicative considering the high casein concentration and the preferential shift into curd.

Further studies are ongoing to investigate the behaviour of Pb especially to understand whether its possible link with proteins could determine an increase of the Pb different from the mere concentration factor from milk to cheese.

# Proficiency Testing as a Tool to Assess Quality of Data: the Experience of the EU Reference Laboratory for Chemical Elements in Food of Animal Origin

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Quality and reliability of analytical results are, in general, key issues for all laboratories but become a top priority for laboratories accredited according to ISO/IEC 17025:2005 (General requirements for the competence of testing and calibration laboratories). In this international standard the proficiency testing (PT) is regarded as a means to assure the validity of results.

In particular, PT consists in using interlaboratory comparisons for the assessment of theparticipants' performance carrying out the evaluation against pre-established criteria, through comparisons with other laboratories. These tests allow the individual participant to compare their work with that of others, obtaining a feedback on the reliability of their performance or on the need to investigate potential problems.

Nowadays, the proved competence of laboratories is an essential requirement especially for that structures that are involved in the official controls aimed at ensuring the safety of EU food products and the public health. To guarantee the EU consumers, the Council and the Commission have designated a lot of European Union Reference Laboratories (EURLs), whose main role is to contribute to the standardization of analytical methods and to the harmonization of performance among the EU National Reference Laboratories (NRLs) to reach a comparable level of quality in the analytical data among all Member States. With this aim, the organization of PTs is a task that each Reference Laboratory has to accomplish. Over the last fifteen years, the EURL for chemical elements in food of animal origin (EURL-CEFAO) have organized a lot of PTs on determination of total As, Cd, Pb and total Hg in meat, milk, fish and offal for the benefit of its network of NRLs. To make the exercises as profitable for participants as possible the EURL-CEFAO obtained the accreditation as PT provider since 2010 (ISO/IEC 17043:2010). Roughly twenty exercises have been conducted as of 2006 producing materials adequate to the NRLs' needs as well as to the PT purposes.

Some specific aspects of this activity will be discussed (e.g. preparation and characterization of PT materials, statistical evaluation of data, follow-up actions). Finally, based on the EURL-CEFAO experience, it will be demonstrated that the participation into PTs on a regular basis can result in a an improvement of the laboratory's performance as well as in the harmonization of the results submitted by participants.

# Synthesis, In Vitro β-Glucuronidase Inhibitory Activity and In Silico Studies of Novel (E)-4-Aryl-2-(2-(pyren-1-ylmethylene) hydrazinyl)thiazoles

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Current research is based on the synthesis of novel (*E*)-4-aryl-2-(2-(pyren-1ylmethylene)hydrazinyl)thiazole derivatives (**3-15**) by adopting two steps route. First step was the condensation between the pyrene-1-carbaldehyde (**1**) with the thiosemicarbazide to afford pyrene-1-thiosemicarbazone intermediate (**2**). While in second step,cyclization between the intermediate (**2**) and phenacyl bromide derivatives or 2-bromo ethyl acetate was carried out. Synthetic derivatives were structurally characterized by spectroscopic techniques such as EI-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR. Stereochemistry of the iminic double bond was confirmed by NOESY analysis. All pure compounds **2-15** were subjected for *in vitro*  $\beta$ -glucuronidase inhibitory activity. All moleculeswere exhibited excellent inhibition in the range of IC<sub>50</sub> = 3.10 ± 0.10-40.10 ± 0.90  $\mu$ M and found to be even more potent than the standard D-saccharic acid 1,4lactone (IC<sub>50</sub> = 48.38 ± 1.05 $\mu$ M). Molecular docking studies were carried out to verify the structure-activity relationship. A good correlation was perceived between the docking study and biological evaluation of active compounds.


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The Universities of Sapienza, Rome, Italy, and of Salento, Lecce, Italy organized the Eurasia Conference on Chemical Sciences, at the Faculty of Civil and Industrial Engineering Sapienza University of Rome - 5-8, September 2018. This is the 15th Eurasia conference (EuAsC2S-15) and it covers all branches of modern chemistry.

All previous conferences in this series were organized in Asian countries, and only one in Europe, the 12th Eurasia, in Corfu' Greece; thus this is the second conference of the series to be organised in Europe.

After the successful experience of this international series, this conference will bring together leading chemists and young scientists to exchange scientific chemical information. The program includes Plenary and Invited lectures, oral and poster communications.

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