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Dr. Tatiana Chenet, tatiana.chenet@unife.it

E-mail contatto: sci_emiliaromagna@chim.it

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Dr. Barbara Bricoli, GEA Procomac S.p.A., barbara.bricoli@gea.com

Indice

KN1 – DIDATTICA A DISTANZA E CHIMICA: NON TUTTO IL MALE VIEN PER NUOCERE
DISTANCE EDUCATION: NOT ALL EVIL COMES TO HARM

Margherita Venturi
Dipartimento di Chimica "Giacomo Ciamician" – Università di Bologna
Via Selmi n. 2 – 40126 Bologna
E-mail: margherita.venturi@unibo.it

ABSTRACT

It may seem like a paradox, but it really happened: our country needed a pandemic to stir up the interest of the media in education and teaching (even if in a rather restrictive sense). Everyone expressed his idea, sometime strange and unusual, but at least it emerged loud and clear that school is important and that we cannot do without it. Then, almost everyone agreed on the fact that, not being able to physically go to the classroom, we had to move on to distance education. By making this choice, or rather imposition, the teachers had to do it in a hurry, without having been able or able to follow serious and in-depth refresher courses not only on technologies, but also on the most effective way of planning a remote lesson.
Chemistry, which is the most experimental discipline, had suffered a lot from the pandemic situation because the chemistry teachers, in addition to having to prepare effective and engaging remote lessons, had the big problem of laboratory activities, which were interrupted for months in many institutions.
In the face of all these problems, however, the experience gained last year has taught us something, something to treasure by returning to the classroom. So not all evil comes to harm!

KN2 – LYONDELLBASELL: RICERCA & SVILUPPO, SOSTENIBILITA' E RICICLO CHIMICO
LYONDELLBASELL: RESEARCH & DEVELOPMENT, SUSTAINABILITY AND CHEMICAL RECYCLING

Dario Liguori
Basell Poliolefine Italia Srl (gruppo LyondellBasell), Centro Ricerche G. Natta, P.le G. Donegani 12, 44122 – Ferrara
E-mail: dario.liguori@lyb.com

ABSTRACT

As LyondellBasell one of the world's largest producers of plastics and chemicals, our products are used by millions of people around the world, every day. We have the potential — and responsibility — to use this scale and reach to make a positive impact across our value chains. That's why we are working to make meaningful progress to address some of the world's most pressing challenges such as **reducing plastic waste** in the environment, helping to **mitigate climate change** and contributing to a **thriving society** for our employees, the communities where we operate and the people who depend on our products.
Across the world, plastics improve our quality of life and play a critical role in advancing a wide range of sustainability efforts *(e.g., helping to reduce emissions through the light weighting of vehicles; addressing food waste through packaging that extends storage, improving the energy efficiency of buildings, ...)* and therefore plastics play a vital role in addressing all these challenges.
Yet, today, our world faces a large and growing problem in the form of plastic waste in the environment. We believe that finding solutions to this challenge requires collaboration from all parts of the value chain, new partnerships between industry, governments and focused innovation. LyondellBasell is committed to playing an active role in helping to address this critically important challenge for our planet.
On a global basis, LyondellBasell supports a variety of efforts to prevent plastic from entering the environment, among these it is very important to promote and increase more and more the **reuse and recycling of plastic waste** and incentivize the **introduction of new recycling technologies** *(chemical recycling)* to complement existing mechanical recycling technologies.
Globally speaking, mechanical recycling is the most used method for new uses of plastics waste. However mechanical recycling has some limitations and does not allow to obtain many polymeric grades that require particular purity or particular physical/mechanical properties that only virgin polymers can guarantee.
Chemical recycling, on the other hand, reworks the plastic and modifies its structure so that it can be used as a raw material for different industries or raw material for the production of monomers, so as to recreate through polymerization, again virgin polymers and close the circularity. Moreover, very importantly, chemical recycling uses low quality plastic waste that could never be used by mechanical recycling and therefore is the ideal complement to maximize the effectiveness of circularity of plastic materials.
LyondellBasell is actively developing a proprietary chemical recycling technology based on the ***MoReTec*** [1] process (Advanced Recycling Technology).

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[1] *MoReTec* is a trademark owned and/or used by the LyondellBasell family of companies and it is registered in the U.S. Patent and Trademark Office.

KN3 – IL RUOLO DEI BIOMATERIALI IN MEDICINA: DALLA SOSTITUZIONE 'INERTE' ALLA RIGENERAZIONE PERSONALIZZATA

Maria Letizia Focarete
Dipartimento di Chimica "Giacomo Ciamician", via Selmi 2, 40126, Bologna e Centro Interdipartimentale per la Ricerca industriale Scienze della Vita e Tecnologie per la Salute, Università di Bologna. E-mail: marialetizia.focarete@unibo.it

ABSTRACT

I biomateriali rappresentano utili strumenti al servizio della medicina e contribuiscono a migliorare la salute e la qualità della vita di milioni di persone. Ma che cos'è un biomateriale? Un biomateriale viene definito come "un materiale concepito per interfacciarsi con i sistemi biologici al fine di valutare, dare supporto o sostituire un qualsiasi tessuto, organo o funzione del corpo" (definizione stabilita nel corso della II International Consensus Conference on Biomaterials, Chester, Inghilterra, 1991). La storia dei biomateriali è molto antica e parte dall'utilizzo dei materiali che i nostri antenati trovavano attorno a loro (fibre vegetali, legno, tessuti ricavati da animali) per la fabbricazione di protesi o per riparare ferite. La scienza dei biomateriali ha poi avuto una rapida crescita a partire dal secolo scorso, con lo sviluppo e la disponibilità commerciale di nuovi materiali, che ha reso possibile la progettazione di dispositivi con proprietà mirate a specifiche applicazioni in campo medico. Leghe metalliche, alluminio, materiali ceramici e materie plastiche sono quindi diventati largamente utilizzati come biomateriali, anche se non progettati appositamente per l'utilizzo in campo medico. Molti sono gli esempi di queste contaminazioni, come ad esempio l'utilizzo del poliuretano che si utilizzava nei busti e corsetti delle signore come materiale per il primo cuore artificiale.

I biomateriali di prima generazione, il cui requisito fondamentale era di essere bioinerti sono poi stati sostituiti da biomateriali bioattivi (seconda generazione) e infine da biomateriali in grado di supportare e stimolare la rigenerazione di tessuti funzionali (terza generazione). Questa evoluzione è stata possibile grazie alla contaminazione tra chimica, scienza dei materiali, biologia e medicina, in uno stimolante contesto multidisciplinare. I biomateriali sono quindi diventati protagonisti delle cosiddette 'terapie avanzate', che rappresentano una frontiera dell'innovazione in medicina, e comprendono la medicina rigenerativa, l'ingegneria dei tessuti, le terapie cellulari e geniche. In particolare, l'ingegneria dei tessuti rappresenta una promettente alternativa al trapianto di organi, poiché permette di evitare o ridurre al minimo la risposta immunitaria negativa dell'organismo e contribuisce a risolvere i problemi legati alla scarsa disponibilità di organi.

I biomateriali svolgono un ruolo da protagonisti attraverso il loro utilizzo nella stampa 3-D per la fabbricazione di modelli anatomici per la pianificazione preoperatoria, di guide chirurgiche e di impianti personalizzati per protesi, così come nella produzione di tessuti e organi artificiali costruiti a partire da cellule di pazienti mediante la tecnologia del 3D-bioprinting. In questo contesto, i biomateriali, combinati con cellule, con farmaci o con molecole bioattive, permettono l''autoriparazione' dei tessuti nell'ottica della medicina personalizzata. La possibilità di progettare soluzioni terapeutiche e creare sostituiti biologici personalizzati per i singoli pazienti rappresenta l'ultima 'rivoluzione' in medicina e introduce una visione 'paziente-centrica' che aumenta la possibilità di ottenere cure e trattamenti efficaci e promettenti in molti settori.

KN4 – SENSORI CHIMICI: L'ANALISI DIVENTA *SMART*
CHEMICAL SENSORS FOR SMART ANALYSIS

Laura Pigani,[a] Fabrizio Poletti,[a] Barbara Zanfrognini,[a] Chiara Zanardi [a,b]
[a] Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia, via Campi 103, 41125 Modena, Italy
[b] Institute of Organic Synthesis and Photoreactivity (ISOF), National Research Council of Italy (CNR), Via P. Gobetti 101, 40129 Bologna, Italy
E-mail: laura.pigani@unimore.it

ABSTRACT

Sensors are becoming ubiquitous in our daily lives. Early sensors were simple devices, measuring a quantity of interest and producing some form of mechanical, electrical, or optical output signal. In the last decades computing, connectivity to the web, mobile smart devices, and cloud integration have added immensely to the capabilities of sensors.
In particular, chemical sensors have undergone enormous development in recent years and today allow the monitoring of various chemical parameters by combining ease of use, rapid response, portability and cost-effectiveness of the analysis. Applications can be found in environmental monitoring, industrial process monitoring, gas composition analysis, medicine, public security, and on-site emergency disposal. Without replacing conventional laboratory instrumentation, chemical sensors can be effective in all those situations in which *in situ* or online monitoring can allow prompt intervention by the operator, for example in process control, or can constitute a first screening in the identification of samples to be subjected to a more detailed chemical analysis.
Among the most innovative applications we must mention the new frontier of "wearable" sensors, that can be integrated into textile fibers, for monitoring physiological parameters (e.g. electrolytes, glucose and lactic acid) during physical activity.
The research activity of the Elsens group (http://www.elsens.unimore.it/) is dedicated to the development of new electrochemical sensors and biosensors applicable to the analysis of species of interest in the food, environmental and health sectors [1,2].

Figure 1: smart electrochemical sensors' applications

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KN5 – VALORIZZAZIONE DI RESIDUI E SOTTOPRODOTTI DEL COMPARTO AGROALIMENTARE
VALORIZATION OF RESIDUES AND BYPRODUCTS OF THE AGRIFOOD SYSTEM

Stefano Sforza, Tullia Tedeschi
Department of Food and Drug, University of Parma. E-mail: stefano.sforza@unipr.it

ABSTRACT

Achieving optimal nutrition levels for every person in the world is a priority target, but one which is unrealistic given the current food production systems, already putting lot of pressure on the environment. According to FAO, considering the world soil available for agriculture (thus excluding completely unfertile areas), about 30% is already severely degraded and with a high risk of loss of biodiversity, another 10% is moderately degraded, about 45% is stable or slightly degraded, and only about 15% shows signs of improvement. Global population will reach about 9 billion people in 2050. If all these people should access to diets having the same quality and quantity as the ones of the richest areas of the world today, the consumption of resources for food production will be 15 times greater than the present, standing the current production methods.
In a scenario where we need to produce more food, but at the same time in a more sustainable way, by reducing the impact on the environment, food waste reduction, reuse and valorization are certainly pivotal. Today up to one third of the food produced is wasted, amounting to an impressive 1300 Mtons/year. This is the result of linear production systems conceived at a time when resources seemed infinite, as infinite seemed the ability of our environment to "absorb" the final waste. It looks now clear that these production systems must necessarily change, moving away from the linear concept towards "circular" systems where byproducts and discards are to be valorized and re-inserted in the feed/food chain, or used for the production of other goods.
Easy as this concept might seem, valorization of food byproducts and discards is not simple nor straightforward. Agrifood waste is an extremely variable biomass, which includes meat, vegetal, fruits, fish, dairy, lignocellulosic and other discards. The very diverse composition and the tendency to easy spoilage greatly limit both logistic and workability. The techniques for its stabilization, and the extraction and the purification of reusable substances are generally classified as "Direct Biorefinery". A different approach is the so-called "Indirect Biorefinery", in which byproducts are used as a growth substrate for micro-organisms (single cell algae, bacteria) or macro-organisms (insects, algae), yielding a more homogeneous and usually more stable high value biomass, to be used for example for biogas or bioplastics production, or as a source of high value lipids and proteins.
In this lecture, with examples taken from our own research lines, the fundamental and pivotal role of chemists in all these processes, both in direct and indirect biorefinery, will be underlined. Chemists, with their unique "molecular" view, complement in an essential way the other professionals involved (biologists, biotechnologists, food/feed technologists, process engineers and others). The roles played by chemists span from the characterization of raw byproduct materials, to properly assess potentialities and threats of the compounds there contained, to test and developing proper chemical and enzymatical processes aimed at obtaining new quality products, to the final quality and safety assessment of the products obtained.
Examples presented in this lecture will concern many diverse animal and vegetal byproducts and residues, also including insect biomasses as a specific example of indirect valorization of food waste, and will include the complete molecular description of protein and fiber composition of the different biomasses, the set up of methods for protein extraction and fractionation, also involving enzymes, the study of the impact of different processes on protein and lipid quality, the use of chemical reactions directly on the biomasses in order to achieve new desired properties, the evaluation of the content of dangerous compounds in the new products obtained, and the assessment of the allergenic risk in the new products, including the development of processing methods to reduce it.

O1 – A STABLE HIGH-CAPACITY LITHIUM-ION BATTERY USING A BIOMASS-DERIVED SULFUR-CARBON CATHODE AND LITHIATED SILICON ANODE

Vittorio Marangon,[a] Celia Hernández-Rentero,[b] Mara Olivares-Marín,[c] Vicente Gómez-Serrano,[d] Álvaro Caballero,[b] Julián Morales,[b] Jusef Hassoun [a,e,f]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via Fossato di Mortara 17, Ferrara 44121, Italy

[b] Department of Química Inorgánica e Ingeniería Química, Instituto de Química Fina y Nanoquímica, University of Córdoba, 14071 Córdoba, Spain

[c] Department of Ingeniería Mecánica, Energética y de los Materiales, University of Extremadura, Centro Universitario de Mérida, 06800 Mérida, Spain

[d] Department of Química Inorgánica, Facultad de Ciencias, University of Extremadura, 06006 Badajoz, Spain

[e] Graphene Labs, Istituto Italiano di Tecnologia, Via Morego 30 – 16163 Genova, Italy

E-mail: mrnvtr@unife.it (Vittorio Marangon), hssjsf@unife.it (Jusef Hassoun)

ABSTRACT

A full lithium-ion-sulfur cell with a remarkable cycle life was achieved by combining an environmentally sustainable biomass-derived sulfur-carbon cathode and a pre-lithiated silicon oxide anode. X-ray diffraction, Raman spectroscopy, energy dispersive spectroscopy, and thermogravimetry of the cathode evidenced the disordered nature of the carbon matrix in which sulfur was uniformly distributed with a weight content as high as 75%, while scanning and transmission electron microscopy revealed the micrometric morphology of the composite. The sulfur-carbon electrode in the lithium half-cell exhibited a maximum capacity higher than 1200 mAh g_S^{-1}, reversible electrochemical process, limited electrode/electrolyte interphase resistance, and a rate capability up to C/2. The material showed a capacity decay of about 40% with respect to the steady-state value over 100 cycles, likely due to the reaction with the lithium metal of dissolved polysulfides or impurities including P detected in the carbon precursor. Therefore, the replacement of the lithium metal with a less challenging anode was suggested, and the sulfur-carbon composite was subsequently investigated in the full lithium-ion-sulfur battery employing a Li-alloying silicon oxide anode. The full-cell revealed an initial capacity as high as 1200 mAh g_S^{-1}, a retention increased to more than 79% for 100 galvanostatic cycles, and 56% over 500 cycles. The data reported herein well indicated the reliability of energy storage devices with extended cycle life employing high-energy, green, and safe electrode materials.

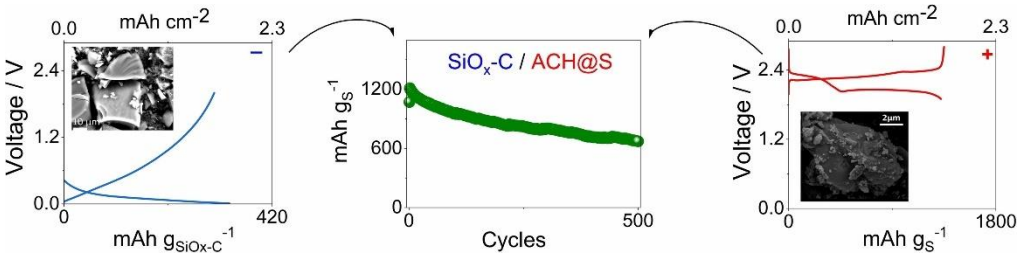

Figure 1. Cycling behavior of the full lithium-ion-sulfur battery (central panel) using a biomass-derived sulfur-carbon cathode (voltage profile and SEM image displayed in the right panel) and a lithiated silicon anode (voltage profile and SEM image exhibited in the left panel).

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O2 – NANOSTRUCTURED Cu-BASED CATALYSTS ON A CARBONACEOUS GAS DIFFUSION MEMBRANE WITH CATALYTIC ACTIVITY FOR CO_2 ELECTROREDUCTION

Martina Serafini, Federica Mariani, Andrea Fasolini, Erika Scavetta, Francesco Basile and Domenica Tonelli
Department of Industrial Chemistry "Toso Montanari", University of Bologna, Viale del Risorgimento, 4, 40136 Bologna, Italy
E-mail: martina.serafini6@unibo.it

ABSTRACT

Among the most promising strategies in view of a substantial industrial revolution in the way energy is produced and converted, the electrochemical reduction of CO_2 to high added-value chemicals is an emerging technology capable of closing the carbon cycle using energy preferably gained from the renewables. For this purpose, Cu has been overall recognized as the gold standard among pure metal catalysts due to its very high selectivity towards hydrocarbons production [1-2] and, coupled with carbonaceous supports, it represents a good candidate for the development of low-cost platforms for a sustainable future.
In this contribution, a set of nanostructured Cu catalysts has been loaded over a carbonaceous gas diffusion layer (CP) by simple and highly reproducible procedures, tuning the morphologies of the materials and the active redox couples with the aim to improve the reaction selectivity [3]. In particular, starting from an electrodeposited 4 cm^2 sized Cu^0 thin layer (**Cu^0**/CP), three different electrocatalysts were obtained by further chemical or electrochemical oxidative treatments: **Cu_2O-Cu^0/CP**, **CuO_x-Cu^0/CP** and **$Cu(OH)_2$-Cu^0/CP** (Figure 1a). The catalytic performances of each electrocatalyst during the liquid phase CO_2 electroreduction were tested in a H-type cell, were an Ag/AgCl electrode and a Pt gauze were used as reference and counter electrodes, respectively, employing 0.3 M $KHCO_3$ as supporting electrolyte. The morphology obtained with the electrochemical treatment (Cu_2O-Cu^0/CP) guarantees a vast electrochemical interface for CO_2 activation and it was demonstrated that the Cu^I/Cu^0 was the most active redox Cu couple as it shows the best productivity and Faradaic Efficiency (FE). Indeed, at -0.4 V *vs* RHE, a productivity of 308 µmol g_{cat}^{-1} h^{-1} and a FE of 76% were obtained for acetate production, which was the main identified product (Figure 1b).

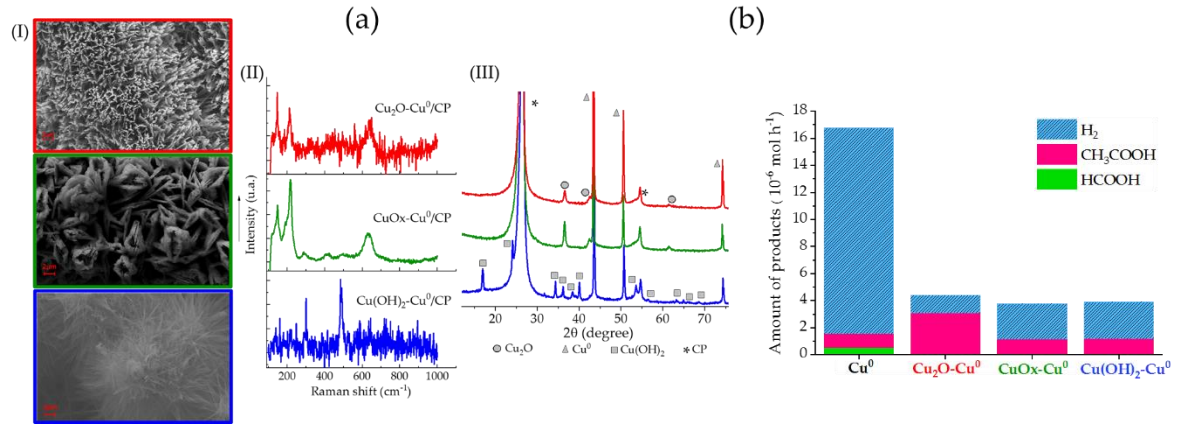

Figure 1. (a) SEM (I), Raman (II) and X-ray diffraction (III) analyses of the oxidized electrocatalysts; (b) Catalytic performances of each catalyst at -0.4V vs RHE, 1h reaction.

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O3 – RECENT DEVELOPMENTS ON THE CHEMICAL COMPOSITION AND BIOACTIVITY OF NON-PSYCHOACTIVE *CANNABIS SATIVA* L. (HEMP) AGAINST HUMAN CHRONIC DISEASES

Lisa Anceschi,[a,b] Virginia Brighenti,[a] Vittoria Borgonetti,[c] Nicoletta Galeotti,[c] Lorenzo Corsi,[a] Federica Pellati [a]

[a] Department of Life Sciences, University of Modena and Reggio Emilia, Via Campi 103-287, 41125 Modena, Italy; E-mail: lisa.anceschi@unimore.it

[b] Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Via Campi 287, 41125 Modena, Italy

[c] Department of Neuroscience, Psychology, Drug Research and Child Health (NEUROFARBA), Section of Pharmacology and Toxicology, University of Florence, Viale G. Pieraccini 6, Florence, 50139, Italy

ABSTRACT

Cannabis sativa L. is an herbaceous plant belonging to the Cannabinaceae family. Cannabinoids are mainly synthesized in glandular trichomes, which are more abundant in female inflorescences. Among them, the most representative compounds are cannabidiolic acid (CBDA), Δ^9-tetrahydrocannabinolic acid (Δ^9-THCA), and cannabigerolic acid (CBGA). These native acidic cannabinoids undergo a spontaneous decarboxylation under the action of light and heat, leading to the formation of their neutral counterparts, including cannabidiol (CBD), Δ^9-tetrahydrocannabinol (Δ^9-THC) and cannabigerol (CBG). Fiber-type *C. sativa* (also known as hemp) is characterized by a high content of CBD and CBG, and a level of psychoactive Δ^9-THC lower than 0.2%. Recently, the interest in non-psychoactive *C. sativa* extracts is increased due to many biological activities related to cannabinoids and other compound. This study was focused on the chemical characterization and application of non-psychoactive *Cannabis sativa* L. extracts, *in vitro* as antiproliferative agents and *in vivo* in a model of neuropatic pain. The compounds present in different extracts from non-psychoactive *C. sativa* varieties were characterized by means of ultra high-performance liquid chromatography coupled with high-resolution mass spectrometry (UHPLC-HRMS) and the complete quantitative analysis was performed using HPLC-UV. The volatile component of extracts was fully caracherized by GC-FID and GC-MS. As to the antiproliferative activity, the K562 chronic myelogenous leukemia cell line was the most sensitive to the treatment and the CBD-type ethanolic extract was the most effective. The antiproliferative effect was mainly due to the induction of apoptosis, but the mechanism of cell death did not involve the main pro- and anti-apoptotic markers such as p53, Bcl-2 and Bcl-xl. The extract was able to increase the cytoplasmatic levels of Cytochrome *c*. Moreover, caspase 3 and 7 seemed to be involved in the mechanism of apoptosis.
C. sativa olive oil extracts with or without terpenes were then tested in an animal model of peripheral neuropathic pain (spared nerve injury) in order to evaluate the analgesic effect of the extracts as well as their role in neuroinflammation and microglial activation. The results suggested that cannabinoids and terpenes may act sinergistically to enhance the bioactivity of the phytocomplex.

O4 – BEYOND THE NUMBERS: A CHEMOMETRIC JOURNEY THROUGH COCRYSTALLIZATION

Fabio Fornari,[a] Fabio Montisci,[a] Federica Bianchi,[a,b] Marina Cocchi,[c] Claudia Carraro,[a] Francesca Cavaliere,[d] Pietro Cozzini,[d] Francesca Peccati,[e] Paolo Pio Mazzeo,[a,f] Nicolò Riboni,[a] Maria Careri,[a,g] Alessia Bacchi [a,f]

[a] University of Parma, Department of Chemistry, Life Sciences and Environmental Sustainability, Parco Area delle Scienze 17/A, Parma, Italy (fabio.fornari@unipr.it, fabio.montisci@unipr.it, federica.bianchi@unipr.it, claudia.carraro@unipr.it, paolopio.mazzeo@unipr.it, nicolo.riboni@unipr.it, maria.careri@unipr.it, alessia.bacchi@unipr.it)

[b] University of Parma, Interdepartmental Center for Packaging (CIPACK), Parco Area delle Scienze, Parma, Italy

[c] University of Modena and Reggio Emilia, Department of Chemical and Geological Sciences, Via Giuseppe Campi 103, Modena, Italy (marina.cocchi@unimore.it)

[d] University of Parma, Department of Food and Drug, Parco Area delle Scienze 17/A, Parma, Italy (francesca.cavaliere@unipr.it, pietro.cozzini@unipr.it)

[e] Basque Research and Technology Alliance (BRTA), Center for Cooperative Research in Biosciences (CIC bioGUNE), Bizkaia Technology Park 801A, Derio, Spain (fpeccati@cicbiogune.es)

[f] University of Parma, Biopharmanet-TEC, Parco Area delle Scienze 27/A, Parma, Italy

[g] University of Parma, Interdepartmental Center on Safety, Technologies, and Agri-Food Innovation (SITEIA.PARMA), Parco Area delle Scienze, Parma, Italy

ABSTRACT

Crystal engineering is a branch of solid-state chemistry which allows for the manipulation of the solid-state structure of matter with the aim of tuning its physicochemical properties. In this context, cocrystallization is an interesting approach frequently used to tune the physicochemical properties of the molecule of interest by trapping it and other suitable partner molecules (coformers) in a single crystal lattice [1]. Although cocrystals have been studied for over 160 years [2], the selection of coformers still represents the major hinder to cocrystal discovery. Hence, the development of cocrystalline forms in pharmaceutics, agrochemistry, and nutraceutics [3] is very costly in terms of time, reagents, and analyses for the characterization of the products.

In this study we explored the use of chemometrics to aid the discovery of binary cocrystalline forms of the active molecules of essential oils, well-known high valuable chemicals [4,5], to enwiden their field of application. We followed the basic idea of the Quantitative Structure-Property Relationship: a Partial-Least Squares–Discriminant Analysis model able to discriminate mixtures and cocrystals based on the molecular descriptors of the partner molecules was calculated, thus strongly reducing the experimental costs. The key point of the developed methodology is the extraction of relevant information also from data of failed cocrystallization experiments, as well as the use of a dataset of chemically diverse molecules. The obtained model exhibited a correct classification rate of 83% on the test set, showing a match of 62% between the predicted and experimental data of cocrystals prepared *via* a variety of methods of a completely external dataset.

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F01 – 1,2-DIMETHOXYETHANE AS ALTERNATIVE SOLVENT TO ACETONITRILE FOR THE SEPARATION OF PHARMACEUTICALLY RELEVANT PEPTIDES

Desiree Bozza,[a] Alessandro Buratti,[a] Giulio Lievore,[a] Chiara De Luca,[b] Simona Felletti,[a] Marco Macis,[c] Antonio Ricci,[c] Walter Cabri,[d] Alberto Cavazzini,[a] Martina Catani [a]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Ferrara 44121, Italy

[b] Department of Environmental and Prevention Sciences, University of Ferrara, Ferrara 44121, Italy

[c] Fresenius Kabi iPSUM Srl, I&D, Villadose (Rovigo) 45010, Italy

[d] Department of Chemistry "Giacomo Ciamician", Alma Mater Studiorum, University of Bologna, Bologna 40126, Italy; Fresenius Kabi iPSUM Srl, I&D, Villadose (Rovigo) 45010, Italy

E-mail: bzzdsr@unife.it

ABSTRACT

The use of peptides for therapeutic purposes is increasingly growing and they are effectively considered as an innovative class of drugs. The interest in this class of biomolecules is due to their highly specific activity and wide range of bioactivities that can activate in the human body compared to traditional drugs. Pharmaceutical peptides are indeed increasingly used for the treatment of symptoms associated with many diseases, including severe necrotizing of soft tissue infection, hereditary angioedema, secondary hyperparathyroidism in people with chronic kidney disease [1].

The most widely technique used to separate therapeutic peptides in pharma industries is high performance liquid chromatography (HPLC). It is used, in fact, not only for the quality control of drugs but also in downstream processes (i.e., purification of target peptides, analysis of active pharmaceutical ingredients (API), characterization of impurities). Peptides are usually separated in reversed-phase conditions (RP-HPLC), using an apolar stationary phase and a polar mobile phase, which is usually a mixture of water and an organic modifier [2]. Acetonitrile (ACN) has been the preferred organic solvent for RPLC for a long time due to its low viscosity, excellent elution strength, UV-transparency, and good miscibility with water. Nevertheless, ACN is a by-product of acrylonitrile manufacture and its metabolic derivatives (e.g., cyanides) are toxic. For this reason, the replacement of ACN with alternative solvents is one of the priorities of green chemistry [2-3].

This work reports about the use of 1,2 dimethoxyethane, commonly known as Glyme, as an alternative to ACN for the separation and purification of pharmaceutically relevant peptides through preparative liquid chromatography. To the best of our knowledge, this solvent has been never used as a mobile phase in chromatography so far. Our results demonstrate that comparable purity can be obtained with the two solvents, but better resolution of critical impurities and narrower peaks have been observed with Glyme with respect to ACN. In order to shed some light on these findings, fundamental studies have been performed to investigate retention mechanism on hydrophobic stationary phases when using the two different solvents. On the one hand, excess adsorption isotherms have been calculated to get insights on the preferential adsorption of the two solvents on the hydrophobic adsorbent. Retention of target peptide has been investigated in a wide range of compositions of mobile phases by using both ACN/water and Glyme/water mixtures.

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F02 – LIGHTING UP THE ELECTROCHEMILUMINESCENCE OF CARBON DOTS THROUGH PRE- AND POST-SYNTHETIC DESIGN

Sara Rebeccani,[a] Francesca Arcudi,[b] Luka Đorđević,[b] Michele Cacioppo,[c] Alessandra Zanut,[a] Giovanni Valenti,[a] Maurizio Prato,[b,c] and Francesco Paolucci [a]

[a] Dipartimento di Chimica "Giacomo Ciamician", Alma Mater Studiorum - Università di Bologna Via Selmi 2, 40126 Bologna, Italy; E-mail: sara.rebeccani2@unibo.it

[b] Department of Chemical and Pharmaceutical Sciences & INSTM, UdR Trieste, University of Trieste Via Licio Giorgieri 1, 34127 Trieste, Italy

[c] Carbon Bionanotechnology Group Center for Cooperative Research in Biomaterials (CIC biomaGUNE), Basque Research and Technology Alliance (BRTA) Paseo de Miramón 182, 20014 Donostia San Sebastián, Spain

ABSTRACT

Electrochemiluminescence is a luminescent phenomenon induced by an electrochemical stimulus. In the last decades, ECL became a very promising analytical technique for clinical applications, mainly thanks to high signal-to-noise ratio. In order to generate electrochemically the excited state, two different precursors, i.e. luminophore and co-reactant, are required. In the quest for ever-increasing sensitivities, ECL can ideally be coupled to nanotechnology to develop new systems and strategies for analyte determination even in very complex matrices.

[1] Nanotechnologies, as dye-doped nanoparticles and Bodipy Carbon Nanodots (BCDs), can improve the sensitivity and sensibility of ECL technique thanks to their advantageous and tuneable properties. [2] They exploit different strategies for increasing the ECL signal intensity. Dye-doped silica nanoparticles concentrate a huge number of dyes, protected by the external environment, in a single nanoparticle. Moreover, they are easily synthesized, hydrophilic and prone to bioconjugation thanks to silica chemistry. [3]

BCDs are Carbon Nanodots functionalized with boron-dipyrromethene (Bodipy). Carbon Dots are a class of photoluminescent and electrochemiluminescent nanomaterials, specifically carbon-based nanoparticles, with ECL elusive properties. Here we focus our attention on ECL proprieties of BCDs and how pre- and post-synthetic design strategies improve the ECL emission properties, opening new opportunities for exploring CDs in biosensing applications. BCDs are excellent candidates as an alternative to $Ru(bpy)_3^{2+}$ luminophores thanks to their features, such as nontoxicity, chemical inertness, high resistance to photobleaching and unique ECL properties. [4]

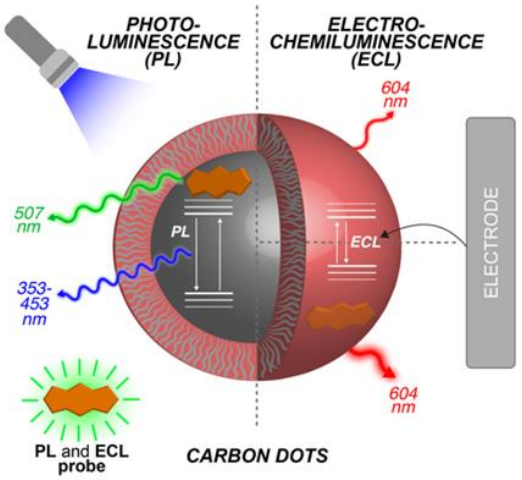

Figure 1. Schematic representation of the ECL and PL mechanism of Bodipy Carbon Nanodots

The final goal is the development of an efficient ECL nanomaterial with high ECL intensity and simple bioconjugation. The study conducted will open new opportunities for exploring CDs in biosensing applications.

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F03 – TUNING THE CATALYTIC CORE OF ARGET ATRP TOWARDS SCALABLE SYNTHESES OF TELECHELICS

Niccolò Braidi, Francesca Parenti
University of Modena and Reggio Emilia, Dpt. of Chemical and Geological Sciences, Italy
E-mail: niccolo.braidi@unimore.it, francesca.parenti@unimore.it

ABSTRACT

Activators Regenerated by Electron Transfer Atom Transfer Radical Polymerization (ARGET ATRP) belongs to a wider class of radical polymerizations that exploits Reversible Deactivation (RDRP). What made RDRP thrive among scientists over the past three decades revolves around the ability to synthesize polymers with both predetermined molecular weight distributions (MWD) and complex macromolecular architectures. This peculiar feature is not achievable in traditional radical polymerizations due to radical–radical termination reactions. By exploiting the reversible deactivation of the propagating radicals, RDRP establishes a dynamic equilibrium and, by shifting it towards the deactivated species, greatly hinders radical–radical terminations. [1] Furthermore, the chain-end functionalities of deactivated polymers are preserved and can be utilized for post-polymerization functionalizations. In pursue of a scalable ARGET ATRP of styrene, we tuned a system that employs a bifunctional initiator thus yielding linear chains with the same functionality at both chain-ends (telechelic halo-terminated polystyrene, **Figure**). The main advancement of our system resides in the use of a green ethyl acetate/ethanol mixture with ascorbic acid (AA) and Na_2CO_3 as the regenerating system. Notably, we found that Na_2CO_3 acts both as the necessary base to deprotonate AA to ascorbate (which in turn is able to reduce X-Cu^{II}/L), and as a promoter of polymerization in absence of AA. [2] The obstacles to the scalability of this system reside principally in the heterogeneity of the mixture (due to the insolubility of the regenerating system) and in the formation of unexpected, branched structures. To contextualize the latter, the emergent competition in ARGET ATRP from a bifunctional initiator can be seen in **Figure**. Since in styrene polymerization radical–radical terminations occur almost exclusively by coupling, given telechelic growing polystyrenes, we can envision the formation of longer, terminally active chains by intermolecular radical–radical coupling as well as the formation of cyclic species by intramolecular radical–radical coupling. [3] We hypothesized that these cyclization reactions can lead to topologically branched/crosslinked structures as proposed for Olympic networks. [4] To overcome the obstacles of the mixture heterogeneity and unexpected branching formation, a homogeneous system was developed. [5] In this communication, we demonstrate that the use of a milder reducing system, suitable also for scalability from lab to batch scale, helps to greatly reduce couplings. To support the reaction design, we made use of experimental design and showed how the catalytic core can be tuned to obtain telechelic halo-terminated low-MW polystyrene with predetermined MWD.

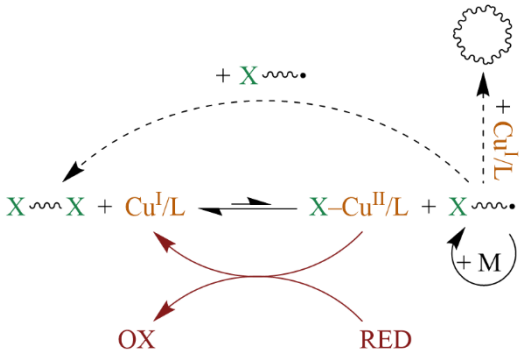

Figure Emerging three-way competition from the use of a bifunctional initiator in ARGET ATRP of styrene (propagation, inter- and intra-molecular couplings). The variables studied to assess scalability of the system are colored.

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F04 – DEVELOPMENT OF SMART AND PORTABLE IMMUNOSENSOR FOR DETECTION OF SARS-COV-2 SPIKE PROTEIN IN NASOPHARYNGEAL SWABS

Chiara Giliberti,[a] Simone Fortunati,[a] Angelo Bolchi,[a] Davide Ferrari,[a] Valentina Bianchi,[b] Ilaria De Munari,[b] Andrea Boni,[b] Marco Giannetto,[a] Maria Careri,[a]

[a] Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parco Area delle Scienze 17/A, 43124, Parma, Italy. E-mail: chiara.giliberti@unipr.it

[b] Department of Engineering and Architecture, University of Parma, Parco Area delle Scienze 181/A, 43124, Parma, Italy

ABSTRACT

The social impact of SARS-CoV-2 pandemic has brought an increasing need for easy-to-use and rapid diagnostic devices, suitable for non-hospital settings, aimed at identifying SARS-CoV-2 positive subjects. In this context, we developed an immunoassay based on disposable screen-printed electrodes functionalized with monoclonal antibodies to detect the presence of S1 subunit of Spike viral protein in nasopharyngeal swabs to track positive subjects. The acquisition device is portable and battery-operated and is designed to acquire data using a potentiostat devised by the Department of Engineering and Architecture of University of Parma; these datasets can be sent to a Cloud platform and processed using wireless connection, making the device consistent with the concept of "Internet of Things" (IoT) [1]. Monoclonal anti-S1 IgM antibody was immobilised on the electrode's surface as receptor, while the antigen was detected using a Rabbit Polyclonal Antibody, which in turn is detected by Goat anti-Rabbit secondary antibody tagged with alkaline phosphatase (GAR-AP) using the enzyme substrate hydroquinone diphosphate (HQDP). The substrate is converted into hydroquinone and then it undergoes electrochemical oxidation to generate the signal of analytical interest obtained by differential pulse voltammetry [2]. Viral Transport Medium (VTM) was used as a matrix to simulate the test conditions. A Full Factorial Design with two factors and three levels was applied to optimize IgM and Polyclonal Antibody concentrations. the best conditions being 15 µg/ml and 1 µg/ml for IgM and for polyclonal antibody concentration, respectively. Optimized conditions were used to assess the analytical performance of the immunoassay, obtaining LOD and LOQ values of 12 ng/µl and 40 ng/µl, respectively. Furthermore, cross-reactivity tests were carried out using H1N1 Hemagglutinin (HA) from influenza A virus and Spike Protein (S1) from MERS Coronavirus: our findings showed the absence of interference for both MERS S1 and H1N1 HA, with a signal comparable to the negative sample from the immunoassay developed. The high selectivity for SARS-CoV-2 viral antigen coupled with the low levels of LOD and LOQ make the immunosensor valuable for IoT devices for the rapid detection of SARS-CoV-2 positive subjects.

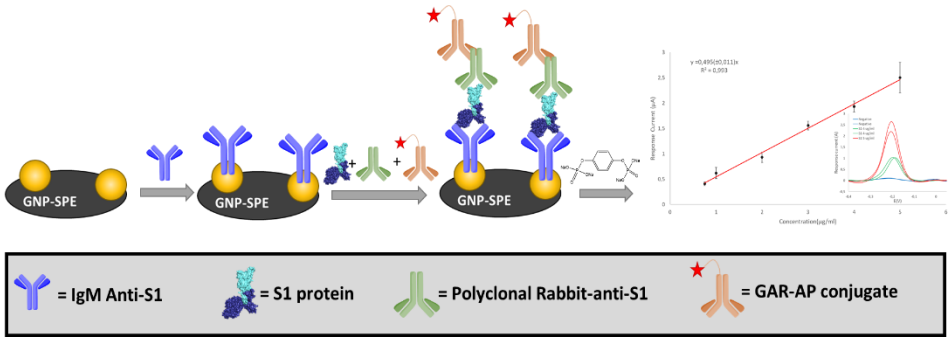

Fig.1 Immunoassay setup

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F05 – DESIGN AND SYNTHESIS OF MULTITARGET-DIRECTED LIGANDS TO TACKLE NEUROINFLAMMATION

Giambattista Marotta,[a] Rita Maria Concetta Di Martino,[b] Debora Russo,[c] Ilaria Penna,[c] Michela Rosini,[a] Jose Antonio Ortega,[b] Anna Minarini [a]

[a]Department of Pharmacy and Biotechnology, Alma Mater Studiorum – Università di Bologna, via Belmeloro, 6 - 40126 Bologna (IT)

[b]Computational and Chemical Biology, Italian Institute of Technology, 16163 Genova (IT)

[c]D3 Pharma Chemistry Line, Italian institute of Technology, 16163 Genova (IT)

E-mail: giambattista.marott2@unibo.it

ABSTRACT

Neuroinflammation is a chronic pathological condition of Alzheimer's disease fostered by the deposition of β-amyloid (Aβ) peptide and of hyperphosphorylated tau protein (τ), ultimately leading to neuronal death. Persistent accumulation of Aβ is responsible for the activation of astrocytes and microglia[1] and for the stimulation of different protein kinases, among which Gsk-3β and Fyn. Chronic stimulation of these two kinases activates a cascade of events culminating in the transcription of pro-inflammatory genes and in the hyperphosphorylation of τ, which is no longer able to ensure axonal transport, thus leading to neuronal death.[2,3] In addition, persistently-activated Fyn promotes excitotoxicity due to the interaction with NMDA receptors (NMDARs).[3]

Given that neuroinflammation is sustained by various interconnected pathological mechanisms, it may be insufficient to hit a single biological target, therefore different pharmacological approaches have been developed over time, such as the multitarget ligands, namely single molecules capable of simultaneously binding to two or more targets.[4]

In this context, through a virtual screening study we identified hit compound **1** based on a 7-azaindole-3-aminothiazole structure (figure 1) with a dual inhibitory activity on Gsk-3β and Fyn, albeit unbalanced towards the former. Therefore, we undertook a hit-optimization work in order to obtain an improved and more balanced activity on both kinases by synthesizing a small set of derivatives bearing various aliphatic and aromatic substituents on the aminothiazole moiety as well as on the azaindole core. Also, as a continuation of this work, we replaced the aminothiazole ring with cyclic analogues to figure out how this replacement would affect the activity. *In vitro* inhibition assays allowed us to elucidate compound **1**'s structural features required for a dual profile on target kinases and represents a starting point for outlining the structure-activity relationships of this class of compounds.

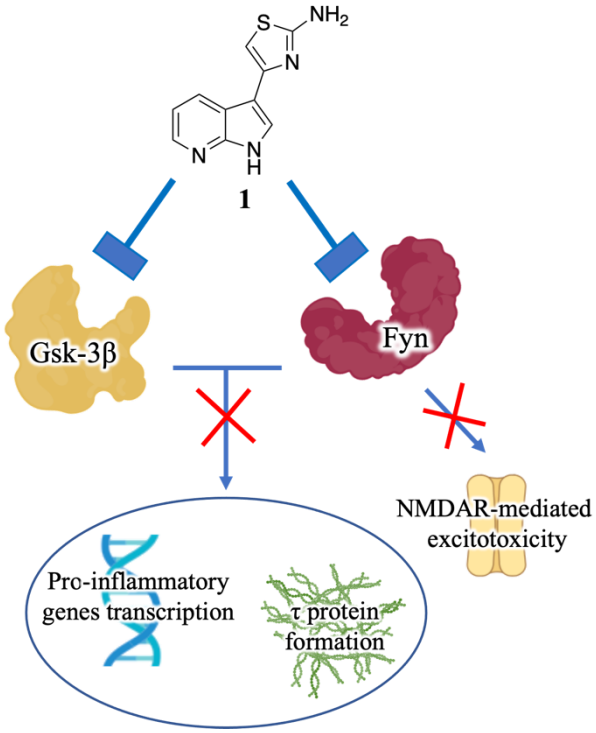

Figure 1. 7-azaindole-3-aminothiazole **1** as dual ligand of Gsk-3β and Fyn.

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F06 – PROOF-OF-CONCEPT STUDY ON THE APPLICATION OF THE INVERTED CHIRALITY COLUMN APPROACH FOR THE SEPARATION OF CHIRAL CANNABINOIDS THROUGH HIGH PERFORMANCE LIQUID CHROMATOGHRAPHY

A. Buratti,[a] S. Felletti [a] M. Catani,[a] D. Bozza,[a] C. De Luca,[b] G. Lievore,[a] F. Pellati,[c] V. Brighenti,[c] F. Gasparrini,[d] A. Cavazzini [a]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Ferrara 44121, Italy; E-mail: brtlsn3@unife.it

[b] Department of Environmental and Prevention Sciences, University of Ferrara, Via L. Borsari 46 44121, Ferrara, Italy

[c] Department of Life Sciences, University of Modena and Reggio Emilia, Modena 41125, Italy

[d] Department of Drug Chemistry and Technology, "Sapienza" University of Rome, P. le Aldo Moro 5, Rome 00185, Italy

ABSTRACT

In recent years, the Cannabis sativa L. plant has seen its use growing exponentially for both medically purposes and as a source of textile fiber. However, its use has also been much debated due to its psychoactive properties [1]. In this regard, the study of its chemical components and pharmacological properties has become a critical point of study for the correct classification of cannabis-based products [2]. Currently, the number of naturally occurring cannabinoids identified is over 100, but a drastic increase of this number is expected. Another very important feature of cannabinoids is that most of them are chiral and, as is typically the case with natural products, the plant synthesizes a single enantiomer ((that is (-)-L-*trans* form). However, cannabis extracts are very complex mixtures and in most of the cases minor enantiomers are not available as standard [3]. One of the most promising approaches for the separation of chiral compounds when the standard solution are not commercially available is the "Inverted Chirality Column Approach" (ICCA). This method is based on the use of two chiral stationary phases (CSPs) having the same associated selector but with an opposite configuration. This feature allows to reverse the elution order of a given enantiomeric pair. In this work, a detailed study on the retention of seven cannabinoids was conducted. It is possible to use the ICCA approach only for chiral cannabinoids (marked with *), however analyzing achiral cannabinoids. Specifically, seven standards of cannabidivarin* (CBDV), cannabidiol* (CBD), tetrahydrocannabinol* (THC), cannabigerol (CBG), tetrahydrocannabinolic acid* (THCA), cannabichromene* (CBC), cannabidiolic acid* (CBDA) and cannabinol (CBN) were used on two inverted chirality columns, based on (S,S)- and (R,R)-Whelk-O1 CSPs in the sub-2 µm format.

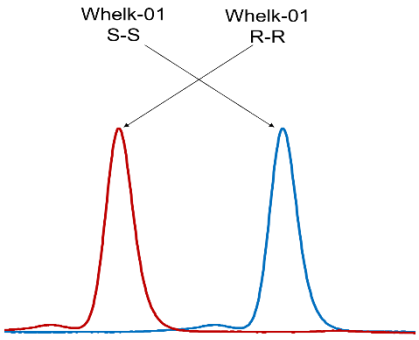

Figure 1 Typical condition obtained using the "Inverted Chirality Columns Approach"

The information obtained from the use of these standards was then used to evaluate the chiral separation in both columns for real cannabis samples of four different cannabis strains. This work is intened as a proof of concept to to demonstrate that the ICCA approach can be effectively employed for real samples analysis, to identify pairs of enantiomers in case they are not available as pure standards.

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F07 – INFLUENCE OF POLY VINYL-ALCOHOL HYDROLYSIS DEGREE ON METAL NANOCATALYSTS FOR THE CATALYTIC CONVERSION OF ORGANIC POLLUTANTS

Stefano Scurti, Filippo Capancioni, Daniele Caretti, Nikolaos Dimitratos
Industrial Chemistry "Toso Montanari" Department, University of Bologna, Viale Risorgimento 4, 40136 Bologna, Italy
E-mail: stefano.scurti2@unibo.it, filippo.capancioni@studio.unibo.it, daniele.caretti@unibo.it, nikolaos.dimitratos@unibo.it

ABSTRACT

In the last years, the management of water is a priority goal for the sustainable development considering the increasing issues related to exhausted water resources, global warming and environmental pollution. In this scenario, the water controlling intended for human consumption derived from underground aquifers or surface reservoirs represents an achievement of crucial importance. In particular the diffused use of aromatic compounds as intermediates in organic synthesis and their strong pollutant nature have created the necessity to develop novel green catalytic treatments to convert pollutants in useful chemical compounds and therefore their removal from the environment represented an important goal because of the negative effects on human and animals.[1] Moreover, inorganic nanostructured materials have emerged as suitable heterogeneous catalysts for the water remediation by catalytic and photo-catalytic treatments. However, a specific design for high-performing nano-catalysts prepared by wet-chemical methodology resulted more complex due to the large number of variables such as the catalytic environment, the dynamic mass- and energy-transport processes and the presence of specific ligands that can bind the surface of nano-catalysts to tune the nanostructures and prevent the aggregation phenomena. The conformation of ligands on a confined NP surface is largely determined by the chain length, the charge and electronic density of ligands and nanoparticles. Furthermore, novel studies have been focused on the effective role of the polymers on the catalytic reduction mechanism in terms of active phase coverage, selectivity tuning and promotion effect mediated by defined functional groups.[2] In particular, PVA exhibits properties such as hydro-solubility, biodegradability and biocompatibility, which are fundamentals to design a catalytic material by synthesis in water media. Based on this premise, in this work the effect of poly(vinyl-alcohol-co-vinyl-acetate) stabilizers in terms of their molecular weight and copolymer composition on preformed gold, palladium and Au-Pd nano-alloy colloidal nanoparticles supported on active carbon (MNPs/AC) was investigated.[3] The 4-Nitrophenol (4-NP) catalytic reduction as well as the Methyl Orange (MO) catalytic degradation with $NaBH_4$ as reducing agent, have been used to investigate the catalytic activity of synthesized nano catalysts. Several characterization techniques have been combined to correlate the properties of the functionalised polymers used as stabiliser, with the average nanoparticle size and finally with the observed catalytic activity and stability.

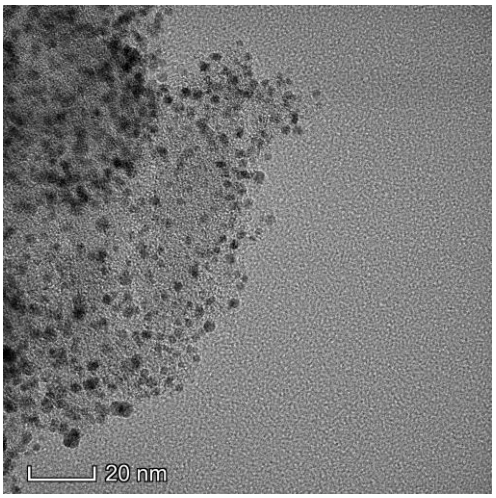

Figure 1: Transmission Electron Microscopy (TEM) image of gold nanoparticles synthesized using PVA fully hydrolysed

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F08 – PROBING THE CHEMICAL SPACE OF DUAL KINASE INHIBITORS: OPTIMIZATION OF SYNTHETIC LINES AND IDENTIFICATION OF NOVEL SCAFFOLDS

L. Destro,[a] M. L. Introvigne,[b,c] V. Crippa,[d] L. Mologni,[d] F. Prati,[c] E. Caselli,[c] A. Zambon [a]
[a] Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia, Via Campi 103, 41125 Modena, Italy. E-mail: lorenza.destro@unimore.it, alfonso.zambon@unimore.it
[b] Clinical and Experimental Medicine PhD Programme, University of Modena and Reggio Emilia, Modena, Italy
[c] Department of Life Sciences, University of Modena and Reggio Emilia, Via Campi 103, 41125 Modena, Italy
[d] Department of Medicine and Surgery, University of Milan-Bicocca, 20900 Monza, Italy

ABSTRACT

FLT3 and **RET** protein kinases (PKs) are often concomitantly activated in acute myeloid leukemia (AML), a type of blood cancer with poor prognosis and limited therapeutic options.[1] The current standard of care includes radiotherapy and chemotherapy, and thus has significant side effects, and the 5-year survival rate for people 20 and older with AML is 26%.[2] The development of dual inhibitors of **RET** and **FLT3** could meet the medical need of the large portion of AML patients showing abnormal activities of both these proteins.
In order to identify new protein kinase inhibitors able to act on both **FLT3** and **RET,** we first evaluated a range of pyrazole-ureas**.** This scaffold has been shown to confer therapeutic efficacy against specific PKs,[3,4] and *in silico* studies prompted the synthesis of a library of simple first generation tool compounds with confirmed activities against both proteins. We thus designed refined compounds with the aim to improve potency and to study the structural features that drive the selectivity of the chemotype for those kinases. To access efficiently the chemical space of our inhibitors, we designed a synthetic pathway with a limited number of high yielding steps, no purification issues and in which the main diversity points are introduced at a late stage to avoid running in parallel too many synthetic steps. Key to this route is a **MW-assisted Suzuki** cross-coupling on the problematic benzo-urea scaffold, which reduces the number of reactions needed to synthesize desired analogues. The introduction of this new synthetic protocol allowed us quick access to several target analogues, enriching our library and allowing us to investigate in depth the chemical space of our **RET**/**FLT3** inhibitors.
In order to identify other possible scaffolds able to target **FLT3** and **RET** of PKIs, we started a collaboration with the research group of the professor F. Prati and E. Caselli at University of Modena and Reggio Emilia aimed at evaluating **boronic compounds** as inhibitors of our target proteins. Boronic compounds are attractive scaffolds for the development of new targeted agents due to their favorable physical-chemical properties such as low lipophilicity, water solubility and stability.[5,6] As kinase-targeting agents, boronic compounds are only scantly reported, thus presenting a relatively unhindered IP landscape.

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F09 – DIRECT, ASYMMETRIC SYNTHESIS OF CARBOCYCLE-FUSED URACILS VIA [4+2] CYCLOADDITIONS: A NONCOVALENT ORGANOCATALYSIS APPROACH

Enrico Marcantonio, Claudio Curti, Franca Zanardi
Department of Food and Drug, Parco Area delle Scienze 27/A, 43124 Parma, Italy
E-mail: enrico.marcantonio@unipr.it

ABSTRACT

Uracil derivatives rich in functional groups represent attractive molecules in the field of medicinal chemistry-oriented synthesis, exhibiting biological activities especially as antivirals.[1] However, these heterocycles are often flattened and C(sp^2)-rich rings. Accordingly, three-dimensional and chiral C(sp^3)-rich fused uracil derivatives containing one or more stereocentres constitute particularly interesting novel chemotypes. Vinylogous reactions constitute a potent tool for the selective functionalization of remote C(sp^3)-H bonds.[2] Thus, the combination of the principle of vinylogy with asymmetric chemical methods for the synthesis of nonracemic carbocycle-fused uracils paves the way to a new exploration area of research.
In this context, recent discoveries showed the unprecedented reactivity of remotely enolizable 6-methyluracil-5-carbaldehydes **1** (Scheme 1), which were able to react with enals after covalent activation by a secondary amine organocatalyst via the intermediacy of an *in situ*-formed *ortho*-quinomethane dienamine.[3]
Herein, we report the development of an asymmetric [4+2] cycloaddition between the vinylogous pronucleophiles of type **1** and nitroolefins, under the strategic exploitation of a noncovalent bifunctional organocatalysis.[4] A series of functional group-rich and chiral carbocycle-fused uracils embedding three contiguous stereocenters were obtained in one-step in good yields, with good enantioselectivities and complete diastereocontrol. Moreover, the ability to provide enantiopure products via simple one-cycle recrystallizations and the possibility to further functionalize these scaffolds without losing their chiral integrity were demonstrated.

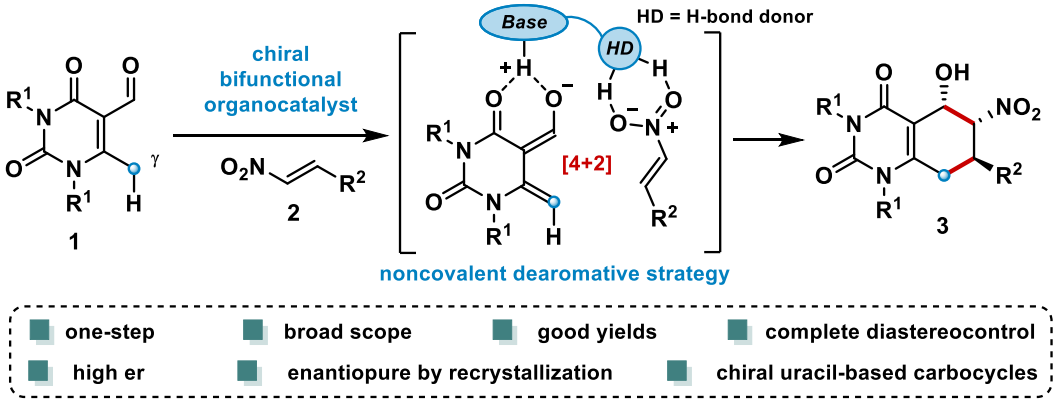

Figure 1 *[4+2] cycloaddition reaction for the synthesis of fused uracil-based heterocycles*

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F10 – ORTHOGONAL NANOARCHITECTONICS OF M13 PHAGE FOR RECEPTOR TARGETED ANTICANCER PHOTODYNAMIC THERAPY

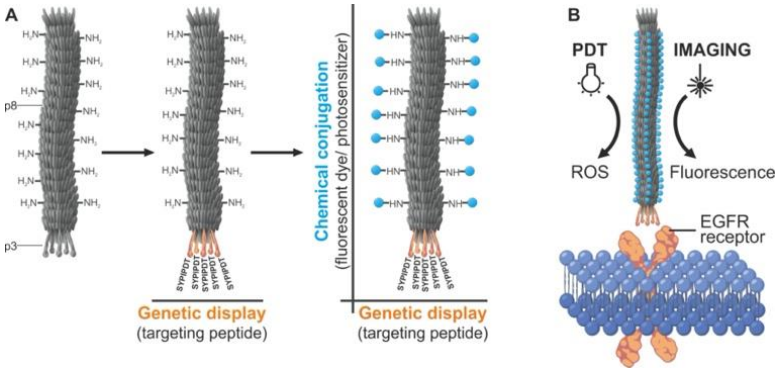
Roberto Saporetti,[a] Luca Ulfo,[b] Andrea Cantelli,[a] Matteo di Giosia,[a] Alberto Danielli,[b] Matteo Calvaresi [a]

[a] Dipartimento di Chimica "Giacomo Ciamician", Alma Mater Studiorum – Università di Bologna, Via Francesco Selmi 2, 40126 Bologna, Italy

[b] Dipartimento di Farmacia e Biotecnologie, Alma Mater Studiorum – Università di Bologna, via Francesco Selmi 3, 40126 Bologna, Italy

ABSTRACT

Photodynamic Therapy (PDT) is a minimally invasive therapy approved in clinical treatment for different types of cancer.[1,2] In PDT cytotoxic reactive oxygen species (ROS) are locally produced by a species, called photosensitizer (PS), upon activation by visible light.[1,2] A selective accumulation of the PS in cancer cells is crucial for minimizing the PDT side effects due to undesired phototoxicity. Therefore, we combined genetic and chemical techniques to engineer M13 bacteriophages obtaining PS vectors for enhanced photodynamic killing targeted against cancer cells, we called this methodology "orthogonal nanoarchitectonics approach".[3] The M13 genetically modified phage displays on the tip a peptide (SYPIPDT) which can bind the epidermal growth factor receptor (EGFR). The redesigned $M13_{EGFR}$ phages demonstrated EGFR-targeted tropism and were internalized by A431 (human squamous carcinoma cell line), which overexpress EGFR. The orthogonal approach consists in chemically conjugating hundreds of Rose Bengal (RB) photosensitizing molecules on the capsid surface of the $M13_{EGFR}$ genetically modified phages, without affecting the selective recognition of the SYPIPDT peptides. This is possible using a cross-coupling reaction between the amino acid amine groups of $M13_{EGFR}$ capsomers and the activated carboxylic-acid group of RB and avoiding the presence of amino groups in the displayed peptide. Upon internalization, the $M13_{EGFR}$-RB derivatives generated intracellularly ROS, activated by an ultralow intensity white light irradiation. The selectivity and the cytotoxicity against cancer cells are so efficient that killing activity is observed at picomolar concentrations of the $M13_{EGFR}$ phage.[3]



A) Orthogonal engineering of M13 phage. M13 phages with targeted tropism against EGFR receptor on the minor coat protein pIII of SYPIPDT peptides. The SYPIPDT peptide does not contain any amino groups that may interfere with the orthogonal functionalization of the virus capsid, that involves amino groups on pVIII for selective chemical conjugation.
B) EGFR targeted anticancer photodynamic therapy and imaging with M13EGFR phage vector.

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P01 – RHEOLOGICAL CHARACTERIZATION OF HYDROXYAPATITE SLURRIES FOR BONE TISSUE REGENERATION

Zahid Abbas,[a,b] Massimiliano Dapporto,[b] Davide Gardini,[b] Simone Sprio [b]
[a] University of Bologna, Bologna
[b] Institute of Science and Technology for Ceramics-National Research Council of Italy (ISTEC-CNR), 48018 Faenza, Italy
E-mai: zahid.abbas@istec.cnr.it

ABSTRACT

The design of hydroxyapatite (HA)-based scaffolds has been widely explored in recent decades as gold standard for the regeneration of large bone defects. However, the fabrication of 3-D scaffolds for load-bearing applications with customized porosity and appropriate mechanical strength still remains a major challenge. The pore-size distribution and pore morphology of scaffolds strongly impact on their bioactivity and osteoconductivity *in vivo*, to provide the environment to promote the cell migration, infiltration, vascularisation, nutrient and oxygen flow to regenerate damaged tissues. Many of the conventional techniques such as sacrificial template, replica and direct foaming are reported to produce porous scaffolds [1]. Furthermore, the 3D bio-printing which involves the extrusion of a bioceramic slurries as a filament following a three-dimensional project, has demonstrated itself to be short of preparing scaffolds with controlled porosity. All these methods are based on the manipulation of slurries which are highly concentrated powder suspensions with critical processing. However, a comprehensive rheological characterization of hydroxyapatite suspensions which provide the fast, precise, controllable, and potentially scalable fabrication is highly desired in this context. The rheological behaviour of HA suspensions must be effectively adapted to process conditions and regulated through adequate disperse phase stabilization, i.e., using proper dispersant amounts to achieve powder homogenization. The calcination of the powder and the amount of dispersant agents significantly affect both the viscoelasticity of the slurry and the final properties of the scaffold [2]. In present research work, hydroxyapatite (HA) suspensions with different powder concentrations (20, 60,100 wt%), calcination treatments (0, 800, 1000°C) and dispersing agent amounts (0.02, 0.2, 2 wt%) were prepared for the evaluation of their influence on the rheological properties. The pH and ζ-potential measurements, as well as viscosity and viscoelasticity tests were used to evaluate the stability of suspensions. Even slight alterations in dispersant concentration can cause substantial changes in rheological characteristics at relatively high solid volume concentration. The calcination temperature had the greatest impact on suspension stability, while a neat transition is observed by dispersant as the powder concentration increased.

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P02 – TEXTILE CHEMICAL SENSORS FOR HEALTHCARE MONITORING

Danilo Arcangeli,[a] Federica Mariani,[a] Isacco Gualandi,[a] Marta Tessarolo,[b] Luca Possanzini,[b] Leo Davide Torchia,[b] Federico Melandri,[c] Domenica Tonelli,[a] Beatrice Fraboni,[b] Erika Scavetta [a]

[a] Department of Industrial Chemistry "Toso Montanari", University of Bologna, Viale Risorgimento 4, 40136, Bologna, Italy; E-mail: danilo.arcangeli2@unibo.it

[b] Department of Physics and Astronomy "Augusto Righi", University of Bologna, Viale Berti Pichat 6/2, Bologna, 40127, Italy

[c] Plastod S.p.A., Bologna, Italy

ABSTRACT

In recent years the necessity for quick, reliable, easy-access and low-cost devices for healthcare assessment has increased steadily, especially during the ongoing SARS-CoV-2 pandemic where the market for such products experienced a fast growth. This contribution deals with a novel class of textile Point-of-Care devices based on poly(3,4-ethylenedioxythiophene):polystyrene sulfonate (PEDOT:PSS) for the detection of chloride concentration and pH [1] in excreted fluids (such as sweat or wound exudate), as well as moisture in the wound bed [2] which are relevant biomarkers linked to the determination of hydration status, diagnosis of cystic fibrosis and wound health status. The use of special textile materials grants the wearability of the device and the continuous, passive and non-invasive sampling of biological fluids, which are still scarcely explored in the medical literature, and could represent the next step in the evolution of personal healthcare monitoring. The sensing layer of the devices was realized by screen-printing a pattern of PEDOT:PSS on medical-grade gauzes. The electrical contacts were made by sewing conductive textile threads. To achieve selectivity towards chloride and pH, Ag/AgCl and Iridium Oxide particles were electrodeposited on the PEDOT:PSS channel by means of electrochemical techniques, while the detection of moisture relied on the intrinsic characteristics of PEDOT:PSS. The determination of the analytes was conducted in both standard solutions and artificial fluids (AF), employing potentiostatic and impedance-based methods while operating in flow conditions by using a HPLC pump, to simulate the spontaneous fluid excretion at 0.05 mL/min. The sensitivities reported for chloride and pH detection were respectively -43.1 ± 0.7 μA decade^{-1} (R^2 = 0.9997; LOD: 0.06 mM) and 59 ± 4 μA pH^{-1} (R^2 = 0.993), while the moisture sensors were capable of reversibly differentiating between a "wet" and "dry" state upon an impedance variation of several orders of magnitude.

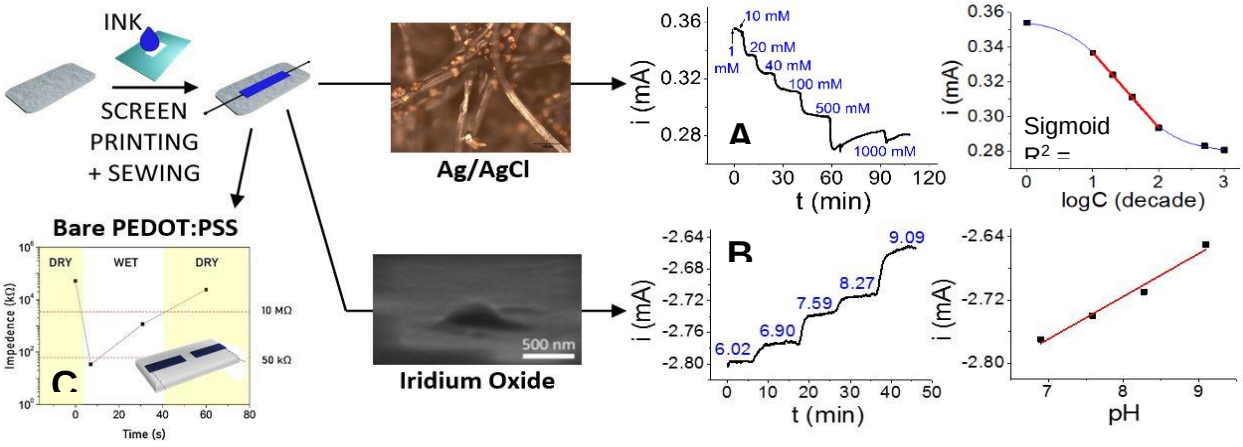

Figure 1. Instrumental response for flow-conditions additions of NaCl in phosphate buffer solution (A) and synthetic wound exudate at various pH (B); punctual artificial sweat addition (C).

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P03 – THE WATER-ENERGY NEXUS IN A DRINKING WATER SUPPLY SYSTEM

Francesco Arfelli,[a] Luca Ciacci,[a] Fabrizio Passarini [a,b]
[a] Department of Industrial Chemistry "Toso Montanari", University of Bologna, viale del Risorgimento 4, 40136 Bologna, Italy
[b] Interdepartmental Centre of Industrial Research "Renewable Resources, Environment, Sea and Energy", University of Bologna, via Angherà 22, 47922 Rimini, Italy

ABSTRACT

Water sustainability is a topic of global interest mainstreamed by the United Nations that, in the "2030 Agenda for Sustainable Development", inserted "Clean water and sanitation" between the SDGs [1]. The balance between drinking water supply and demand implies the investment of resources aimed at optimizing the management of water sources and requires a detailed knowledge of the techniques and operations involved in a drinking water supply system (DWSS). Accordingly, the study consists in the application of the Life Cycle Assessment (LCA) methodology to the DWSS located in the Romagna territory, with the aim to analyze the system as a whole and to compare, from an environmental perspective, different production alternatives related to three water sources (dam water, RD; surface water, SW; and groundwater, GW) and two treatment technologies (conventional and ultrafiltration). This work required the identification and quantification of the main water and energy flows through the Material Flow Analysis (MFA), allowing to provide considerations about the interlinkages and reciprocal dependencies between the two resources (water-energy nexus) in the local context. Despite electricity is essential for drinking water supply, the water sector is responsible for a limited portion of the regional electricity consumption (about 0.5% of the total generated).
Results are reported as a function of 1m^3 of delivered drinking water and following a cradle-to-gate approach. The chosen impact assessment method is ReCiPe 2016 [2]. Despite the influence of the dam infrastructure, the best environmental performances are observed for RD water treated through the conventional technology. Both GW and SW, being them treated in conventional or ultrafiltration plants, resulted in higher impacts. Electricity and aluminum sulfate, which is employed as coagulating agent, resulted the main contributors to the observed values. SW related processes, instead, are highly influenced by the management of the treatment residues. Afterwards, it is confirmed that decreasing the dependency on electricity produced by fossil sources, the environmental impacts observed are remarkably reduced, especially for the global warming category.
The LCA and the nexus analysis are confirmed essential tools to drive companies in addressing environmental-friendly solutions, especially in the field of water sustainability, which represents one of the most urgent challenges to face in the coming years.

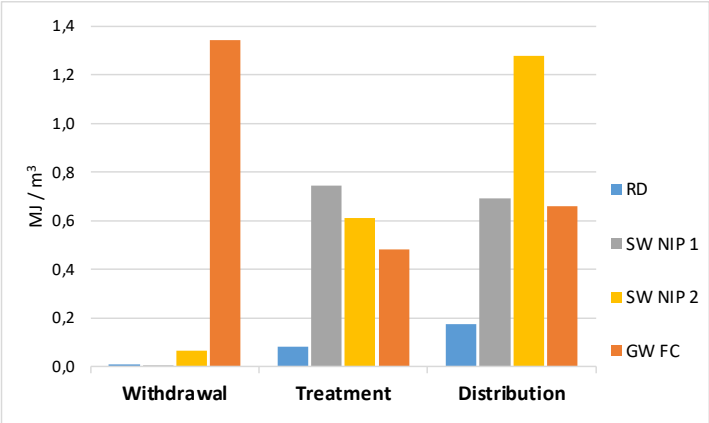

Figura 1: Energy intensity comparison between withdrawal, treatment and distribution processes

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P04 – SYNTHESIS AND CHARACTERIZATION OF NIR CHROMOPHORES FOR PLASMONIC NANOMATERIALS

Silvia Cattani, Beatrice Gatti, Caterina Baccini, Gianpiero Cera, Andrea Secchi
Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/A, 43124, Parma, Italy
E-mail: caterina.baccini@unipr.it

ABSTRACT

Near infrared (NIR) compounds have gained remarkable importance as active materials in several applications, in particular for their use in optical bioimaging. These compounds are suitable candidates to study biological phenomena, since they absorb and emit in the so called "biological window", where body tissues are transparent, and for this reason they can be applied as fluorescent probes.[1] Since the known use of cyanine dyes in optical bioimaging, we chose them as chromophore targets. Despite, the main issue of these compounds is their weak fluorescence intensity. In order to find a feasible solution, a novel approach based on Plasmon-Enhanced-Fluorescence (PEF) effect was developed. Exploiting the optical properties of plasmonic nanostructures, such as Local Surface Plasmon Resonance (LSPR), the fluorescence of the chromophore in proximity of the metallic surface should be enhanced.[2] The project was focused on the synthesis of designed cyanine dyes that can be potentially grafted onto the surface of plasmonic nanomaterials. As most suitable chromophore, heptamethine cyanines were chosen. A terminal thiol or disulfide was introduced at the central core to covalently anchoring the dye to the metallic surface. Derivatives Cy7-NH-C6-O-Lip, Cy7-NH-C11-O-Lip, and Cy7-NH-C11-SH (Figure 1) were first synthesized, and their optical properties were studied by fluorescence analysis. The advantage of nitrogen atom as a linker between the cyanine and the alkylic chain is to gain large Stokes shift values. The main issue of these compounds is due to their absorbance in the visible region of the spectrum and not in the NIR region of interest. A feasible solution is to acetylate the nitrogen atom to obtain a red-shift of the emission band. To this aim, Cy7-NAc-C6-O-Lip and Cy7-NAc-C11-O-Lip (Figure 1) were synthetized and studied: the desired bathochromic shift was observed, together with an undesired smaller Stokes shift value. Therefore, it was promoted the shift at lower energy values by varying the hetero atom linked to the polymethine chain. In particular, a more electronegative atom as sulphur was used with the perspective to obtain a NIR emission. Cyanine Cy-7-S-C10-COOH (Figure 1) was successfully synthetized leading to a bathochromic shift in the NIR region of energy spectrum. Ultimate aim remains to study the PEF effect when chromophore dyes are anchored to the metallic surface of plasmonic nanostructures.

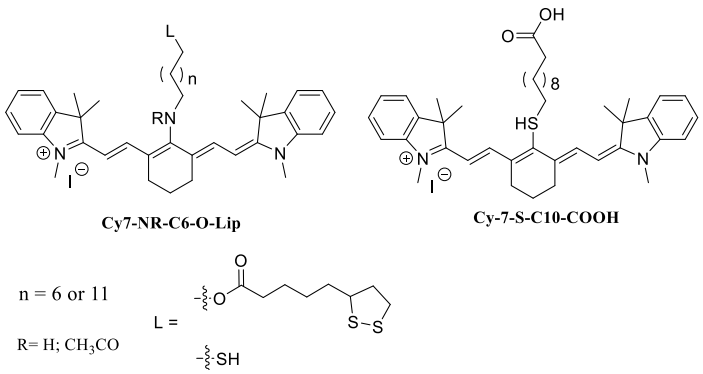

Figure 1. Heptamethine cyanines functionalized with different spacers and linkers.

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P05 – STUDY ON BIOACCUMULATION OF MICROPOLLUTANTS IN TRANSITIONAL WATERS' TROPHIC NETWORK

Andrea Baldi,[a] **Luisa Pasti**,[a] **Leonardo Aguiari** [b]
[a] Department of Chemical, Pharmaceutical, and Agricultural Sciences; University of Ferrara, via Luigi Borsari 46, Ferrara, 44121, Italy
[b] Naturedulis srl, P.zza Leo Scarpa 45, 44020
E-mail: bldndr@unife.it

ABSTRACT

The morphological structure of transitional waters (TWs) and the demi-isolation from the sea make them a privileged habitat for numerous species of flora and fauna. Therefore, TWs are worldwide high valuable ecosystems. Beyond the natural variability, TWs have been long exploited by human activities and among them, with increasing importance, aquaculture. Many of these activities can negatively impact on TWs making them more stressed and prone to deterioration [1].
In addition, because TWs are the end point for freshwater flows (e.g., rivers), they can be affected by inland-produced anthropogenic pollutants, and in particular the ones that show bioaccumulative, persistent and toxic behaviour. The bioaccumulation of these pollutants could be detrimental for aquaculture activities, especially for mussels and bivalve, which are natural filters for water.
Therefore, it is important to study the bioaccumulation and biomagnification of pollutants through the TWs' trophic network to assess the current environmental quality. In addition, predictive approaches based on monitoring data can provide indispensable tools for management policies.
In this preliminary study, Goro's Lagoon (Sacca di Goro) was chosen as representative site. Goro's Lagoon is located in the northern Adriatic Sea at the Po River delta and it is mainly important for the bivalve's aquacultures economies (55% of the overall Italian's bivalve production).
Biotic and abiotic samples were sampled at different times, over two years, near the coast and in the middle of the lagoon. Several classes of pollutants were determined in water, sediments, clams, and algae samples.
Results confirm bioaccumulation of metals like Copper, Zinc, Arsenic, Cadmium and Mercury for clams, as already reported in the literature [2]. In addition, differences were observed in the bioaccumulation of red and green algal species. In particular, the green algae (Ulva Lactuga) show a higher uptake with respect to red algae (Gracilaria).

Figure. The circlet highlights the Goro's Lagoon

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P06 – INVESTIGATION OF CISPLATIN/HYALURONAN COMPLEX IN AN INTRACAVITARY FILM FOR LOCAL TREATMENT OF MALIGNANT PLEURAL MESOTHELIOMA

Sabrina Banella,[a] Eride Quarta,[b] Paolo Colombo,[c] Fabio Sonvico,[b] Luca Ampollini,[b] Fabrizio Bortolotti,[a] Gaia Colombo [a]
[a] Università di Ferrara, [b] Università di Parma, [c] PlumeStars S.r.l.

ABSTRACT

Complete resection of malignant pleural mesothelioma is unlikely and recurrences are frequent. Surgeons use to treat the pleural cavity with anticancer cisplatin (CisPt) solution during thoracic surgery. A hyaluronan-film loaded with CisPt was developed as alternative delivery system for accurate CisPt dosing/application. It is implanted by the surgeon on pleural mesothelium after tumor resection, controlling the dose applied per unit surface.
The film was applied intracavitarily in rats for anticancer efficacy and in sheep to study pharmacokinetics and toxicity. CisPt pharmacokinetics with the film differed from a cisplatin solution injected intravenously or applied intracavitarily, leading to the hypothesis of a circulating complex between CisPt and hyaluronan (NaHA) [1].
This work aimed to assess the interaction between sodium hyaluronate and cisplatin in the film by different techniques. The film was manufactured by layering and drying a mixture of all components. First, Size Exclusion Chromatography-HPLC method allowed to separate NaHA from CisPt, which eluted at 3.7 and 8.5 minutes, respectively. This method qualitatively suggested the CisPt/NaHA complex in the film-forming mixture because only NaHA eluted. The absence of CisPt peak was an indirect evidence of complexation. AAS confirmed that coordinated CisPt was eluted with NaHA and Pt was revealed in the collected NaHA peak fraction.
RP-HPLC quantified about 5% of "free" CisPt in the film-forming mixture, hence 95% of CisPt was complexed [2].
Aiming to investigate the association kinetics between CisPt and NaHA, i.e., the rate to reach the equilibrium of complexation, a film-forming mixture without CisPt was prepared and autoclaved (121 °C, 20 minutes). The thermal treatment drastically reduced the mixture's viscosity, allowing to add CisPt to the system under stirring and follow its concentration over time. After 58 h, only the 10.4±1.0% of CisPt was still free. Conversely, about 90% was associated to NaHA.
Rheology measurements showed that CisPt cross-linked NaHA chains, increasing in the viscosity of mixture. The effect on viscosity was dependent on CisPt concentration.
Understanding how CisPt/NaHA complex may affect drug availability from the implanted film in vivo, was done by in vitro release studies. Drug content in the film complied with the theoretical concentration (1% w/w). CisPt was not released by the film in water, a medium without chloride ions. Moreover, the immersed film rolled up into a cylinder, not dissolving in 48h and longer. This behavior could be caused by non-released coordinated platinum, crosslinking adjacent NaHA chains. In contrast, in the same conditions, a CisPt-free film fully dissolved in 15 min. When the CisPt-film was immersed in NaCl 0.9% (w/v) at 37 °C, the effect of chloride ions on film behavior and cisplatin release rate was neat. Cl- displaced platinum from the complex competing with NaHA carboxylate groups. The film rolled up, like in water, and fully dissolved within 3-4h. Nevertheless, CisPt release was still controlled by the existing complex in solution (90% of CisPt released in 48 h) [2].

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P07 – PREPARATIONS OF POLYLACTIC ACID DISPERSIONS IN WATER FOR COATING APPLICATIONS AND RHEOLOGICAL RESPONSE OF THE FORMULATIONS WITH XANTHAN GUM

Giada Belletti,[a,b] Sara Buoso,[b] Olga Bortolini,[a] Daniele Ragno,[a] Monica Bertoldo [a,b]
[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via L. Borsari 46, 44121 Ferrara (Italy)
[b] Institute of Organic Synthesis and Photoreactivity, National Research Council; Via P. Gobetti 101, 40129 Bologna (Italy)

ABSTRACT

In recent years, in order to produce more eco-friendly products, renewable and biodegradable polymers have been investigated as emerging coating materials. One of the most promising polymers for such a purpose is polylactic acid (PLA) due to its biodegradability, biocompatibility and production on an industrial scale at relatively low cost [1,2,3]. On the other hand, a green, effective methodology for the preparation of sustainable coatings is the use of water-based dispersions or emulsions. Water, indeed, is considered as a cheap, safe, non-toxic and environmentally benign solvent. Accordingly, the preparation and use of water dispersions of poly lactic acid (PLA) for coating purposes is herein presented. The preparation procedure consists in two steps: in the first one, an oil-in water emulsion is obtained by mixing a solution of PLA in ethyl acetate with a water phase containing surfactant and stabilizer. Different homogenization methods as well as oil/water phase ratio, surfactant and stabilizer combinations were screened. In the second step, the quantitative evaporation of the organic solvent provides water dispersions of PLA that are stable, at least, over several weeks at rooms temperature or at 4°C. Particle size was in the 200 nm or 500 nm range, depending on the preparation conditions. The film forming ability of two selected PLA dispersion formulations was studied at different temperatures in the 25-110°C range. With this aim, the formulations were casted and dried onto PTFE capsule and above 60 °C continuous and homogenous PLA film suitable were obtained. Moreover, xanthan gum (XG), a bacterial polysaccharide was studied as possible thickening agent to modulate the viscosity of the formulations. The rheological properties of the PLA dispersions with different XG and PLA contents were studied in steady shear, amplitude sweep and frequency sweep experiments showing the ability of XG in modulating the viscosity of the dispersion without affecting its stability.

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P08 – IN SILICO SCREENING OF NOVEL INHIBITORS OF BETA-LACTAMASES

Laura Bertarini, Andrea Verri, Donatella Tondi
Università degli studi di Modena e Reggio Emilia, Dipartimento Scienze della Vita, via Campi 103, 42125, Modena
E-mail: tondi.donatella@unimore.it

ABSTRACT

Bacterial Resistance represents one of the greatest threats to global health leading to a worrying imbalance between bacterial infections, which are becoming more serious and severe, and available treatments gradually getting ineffective. New resistance mechanisms are emerging and spreading worldwide, making infectious diseases very difficult to treat, if not impossible: as a matter of fact, antibiotic resistance is leading us to a pre-antibiotic era. The most prevalent class of antibiotics used in therapy is represented by beta-lactams, while beta-lactamases are versatile enzymes able to hydrolyze and then to inactivate most of available beta lactams antibiotics. To face this risk and overcome resistance, there is a huge need to discover new antibiotics and effective beta-lactamases inhibitors.
Our study is focused on the identification of novel inhibitors active against KPC-2 and GES-5, beta -lactamases [1-2] belonging to Class A, and NDM-1[3-4], from Class B. We used a computational in silico approach: with the computer software Molecular Docking (GLIDE) we performed a virtual screening on a large library of commercially available compounds, previously filtered for drug likeness properties. Our studies led to novel ligands, chemically characterized by several different moiety (i.e carboxylic acids, tetrazoles and pyrrolidines etc). The performed docking studies were supported by preliminary studies on relevant waters mechanistically involved in beta-lactamase enzymes' hydrolysis mechanism. Flexibility within the active site was also considered for key residues such as Trp105 in KPC-2 and Trp-99 in GES-5.
After further docking validation, the molecules selected in silico as most promising inhibitors that have been now directed to in vitro validation.

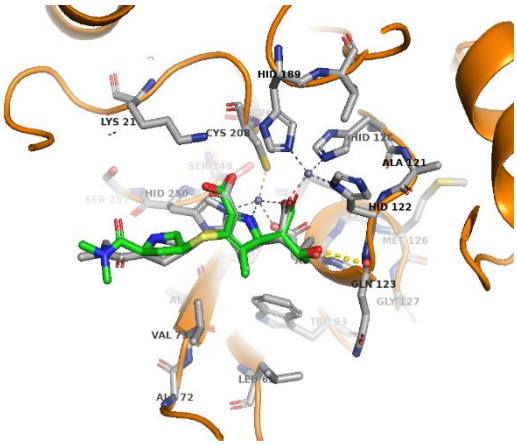

Figure 1. Protocol validation: Crystal structure orientation of Meropenem is shown in white, Meropenem predicted binding conformation in green (PDB ID: 4EYL)

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P09 – LIPID NANOPARTICLES CONTAINING BILE ACIDS FOR THE DELIVERY OF ACTIVE INGREDIENTS: A PRELIMINAR STUDY

Agnese Bondi, Maddalena Sguizzato, Rita Cortesi
Department of Chemical, Pharmaceutical and Agricultural Sciences (DoCPAS), University of Ferrara, Ferrara, Italy

ABSTRACT

In this research Solid Lipid Nanoparticles (SLN) and Nanostructured Lipid Carriers (NLC) containing bile acids in their composition (such as sodium cholate, ursodeoxycholic acid, sodium taurocholate) were studied.
The aim of the research was to verify the ability of such systems in improving the water solubility of lipophilic active molecules proposed for oral administration [1]. As model drug Budesonide was selected.
SLN and NLC prepared by hot homogenization technique followed by sonication [2] are reported in Figure 1. Firstly, a preformulation study on SLN was carried out, enabling to select the amount of bile acid to be used in nanoparticles' composition. Therefore, SLN and NLC, containing 40mg of each different bile acids and 5mg of Budesonide, were produced.
Formulations were dimensionally characterized with Photon Correlation Spectroscopy. The analysis showed that SLN produced have greater mean diameter than NLC but similar polydispersity. Bile acids presence leads to reduction in polydispersity for NLC but not for SLN. In general, SLN showed higher encapsulation efficiency as compared to NLC and emerged a dependence on the type of bile acid used for both SLN and NLC.
In order to verify the ability of these nanosystems to enhance the active ingredient's solubility both in gastric and intestinal fluid, equilibrium dialysis experiments were carried out with two different receiving phases (Fasted State Simulated Gastric Fluid and Fasted State Simulate Intestinal Fluid). The obtained results demonstrated that both SLN and NLC formulations are able to control Budesonide release and improve its solubility in water. Interestingly, all the formulations, except for SLN without bile acids, showed greater release kinetics in FaSSIF than in FaSSGF and NLC with bile acids release Budesonide more rapidly than correspondent SLN in both receiving phases.
In order to study intestinal absorption process, another equilibrium dialysis experiment was carried out, using rat small intestine fragment as a membrane. Both NLC and SLN improved either the solubilisation of the active ingredient and its passage through the gut wall, but NLC showed higher release kinetics than SLN. The experiment was repeated in co-presence of FaSSIF in the intestinal tube, which increased release kinetics of all SLN formulations, whereas for NLC the increase was evident was only for formulations containing ursodeoxycholic acid or sodium taurocholate.

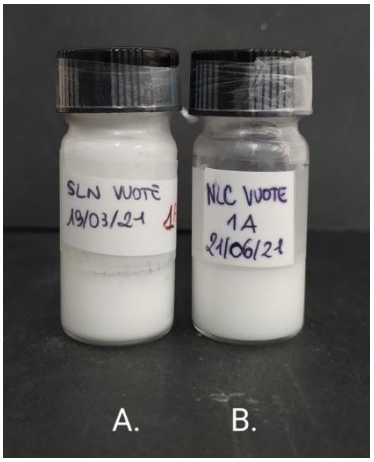

Figure 1. Macroscopic aspect of SLN (A) and NLC (B) formulations

Besides, it was carried out a stability study during time evidencing that bile acids can increase size stability of all the produced SLN and of NLC containing sodium cholate. On the other hand polydispersity index tends to increase with time for all SLN formulations and for NLC depending on the composition. NLC formulations were found to be better in maintaining Budesonide content over time than SLN, which showed variable stability depending on the composition.

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P10 – PHARMACOKINETIC STUDIES OF EUGENOL, CINNAMALDEHYDE AND LIMONENE

Giada Botti,[a] Luca Ferraro,[b] Costanza Leonardi [a] Anna Bianchi [a] Alessandro Dalpiaz [a]
[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via Fossato di Mortara 19, I-44121 Ferrara; bttgdi@unife.it, lnrctn@unife.it, bna@unife.it, dla@unife.it
[b] Department of Life Sciences and Biotechnology, University of Ferrara and LTTA Center, Via L. Borsari 46, I-44121 Ferrara; frl@unife.it

ABSTRACT

Essential oils (EOs) are a complex mixture of volatile compounds produced by aromatic plants as secondary metabolites. EOs are currently studied for their potential therapeutic activity, mainly due to their anti-oxidant and anti-inflammatory properties, possibly useful in the treatment of neurodegenerative disorders, such as Alzheimer's and Parkinson's diseases.
Oral geraniol administration, for instance, has been proposed as a novel therapeutic approach for clinical intervention in Parkinson's disease [1]. We have previously demonstrated that the oral absolute bioavailability of this compound is very high in rats, being about 92%, and that geraniol is able to permeate from the bloodstream to the central nervous system (CNS) [2]. However, being 0.01 the value of the geraniol concentration ratio between the cerebrospinal fluid (CSF) and the bloodstream 30 min after the compound oral administration to rats (corresponding to the C_{max} in the CSF) [2], relatively high oral dosages (up to 200 mg/kg for day) are required to possibly obtain beneficial geraniol central effects [3].
Eugenol, cinnamaldehyde and limonene are known for their anti-oxidant and anti-inflammatory activities, and several studies demonstrated their potential application in the treatment of neurodegenerative disorders [4-6]. The clinical relevance of these findings is, however, limited by the lack of extensive data on their oral bioavailability and their ability to permeate into the CNS from the bloodstream. To possibly contribute to overcome this issue, we performed *in vivo* pharmacokinetic studies by administering eugenol, cinnamaldehyde and limonene to rats. Since EOs are highly lipophilic compounds, appropriate intravenous formulations based on Cremophor®, ethanol and saline solution were necessary to allow their administration at the required amounts and to avoid compound-induced toxicological effects. Corn oil solutions were instead used to orally (gavage) administer the EOs. Eugenol showed an oral absolute bioavailability of 4.25 ± 0.10%, indicating very poor amounts absorbed in the bloodstream from the oral route. On the other hand, 20 minutes after oral administration (corresponding to the C_{max} in the CSF), the concentration ratio between the CSF and the bloodstream of this compound was 0.33 ± 0.02. This value indicates that the ability of eugenol to permeate in the CNS is greater in comparison to that of geraniol (about 30 times higher). Cinnamaldehyde and limonene showed oral bioavailability values of 7.33 ± 0.37% and 7.04 ± 0.96%, respectively, significantly higher than that of eugenol. Cinnamaldehyde was detected in the CSF only after intravenous administration and not when the compound was orally administered. In particular, 10 min after the intravenous administration, the concentration ratio between the CSF and the bloodstream was 0.156 ± 0.038, indicating the ability of cinnamaldehyde to permeate in the CNS from the bloodstream. Limonene, on the other hand appeared totally unable to reach the bloodstream. These findings demonstrate a different ability of the investigated EOs to reach the brain following their oral administration and might be useful to design further studies aimed at evaluating these compounds as potential therapeutic agents for CNS disorders.

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P11 – SELECTIVE SYNTHESIS OF MACROCYCLIC OLIGOESTERS (MCOs) BY OXIDATIVE N-HETEROCYCLIC CARBENE CATALYSIS

Marco Bottin,[a] Daniele Ragno,[a] Graziano di Carmine,[a] Costanza Leonardi,[a] Alessandro Massi,[a] Monica Bertoldo,[a] Olga Bortolini [b]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences (DOCPAS), University of Ferrara, Via L. Borsari 46, 44121-Ferrara, Italy

[b] Department of Environmental and Prevention Sciences, University of Ferrara, Via L. Borsari 46, 44121-Ferrara, Italy

E-mail: marco.bottin@edu.unife.it

ABSTRACT

In recent years, scientific research in the field of polymers has turned to the study of alternative methodologies capable of partially or totally replacing classic synthetic approaches for the production of polymers with high commercial value, through more sustainable processes. To date, a valid alternative to classic step-growth polymerization is represented by ROP *(Ring Opening Polymerization)* [1], a solid synthetic strategy for high molecular weight polymer synthesis, widely used for the production of different polymers such as polyesters, polyamides and polycarbonates. Recently, the entropically driven ring-opening polymerization (ED-ROP) [1] of macrocyclic oligoesters (MCOs) has emerged as an alternative strategy to access a variety of fossil-based and biobased polyesters. While the ROP of small-to-medium size cyclic oligoesters takes place by the relief of the ring strain, the ROP of MCOs proceeds without enthalpy exchange and it is mainly driven by entropy. The widely adopted strategies for MCOs synthesis are cyclodepolymerizations (CDPs) and high dilution condensation (HDC). The latter approach relies on the cyclization of the starting monomers under suitable high dilution conditions (HDC), capable of shifting the equilibrium of the reaction towards cyclization rather than polymerization, according to the *Ziegler-Ruggli Principle* [2]. Given their growing interest in the scientific field, the absence of an organocatalyzed process for MCOs production and our recent contributions in the field [3,4], this work aims to the development of an oxidative N-heterocyclic carbenes (NHCs) promoted strategy for MCOs synthesis (Figure 1). NHCs catalysis allows the use of aldehydes, unlike more activated substrates such as esters and acyl chlorides, under mild conditions and working in the absence of metals, improving process sustainability. In detail, the optimal reaction conditions were investigated in order to provide high selectivity towards cyclic rather than linear species. As model substrates, cyclic oligoesters derived from the coupling of terephthalaldehyde respectively with ethylene glycol $(CET)_n$ and butandiol $(CBT)_n$ were synthetized and characterized. Further investigations aimed at extending this methodology to the synthesis of furan-based polyesters are current underway in our laboratories.

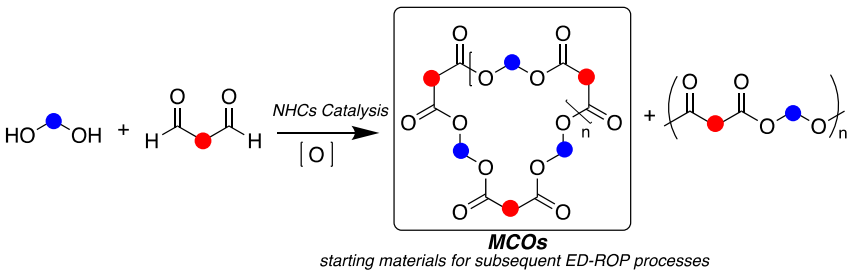

Figure 1. General scheme of MCOs synthesis by NHCs catalysis

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P12 – COVALENT DUAL CONJUGATES TARGETING $\alpha_V\beta_6$ INTEGRIN AND TYROSINE KINASES TOWARD THE TREATMENT OF IDIOPATHIC PULMONARY FIBROSIS

Kelly Bugatti,[a] Elena Andreucci,[b] Lucia Battistini,[a] Franca Zanardi,[a] Francesca Bianchini,[b] Andrea Sartori [b]

[a] Department of Food and Drug, University of Parma, Parco Area delle Scienze 27A, 43124 Parma, Italy

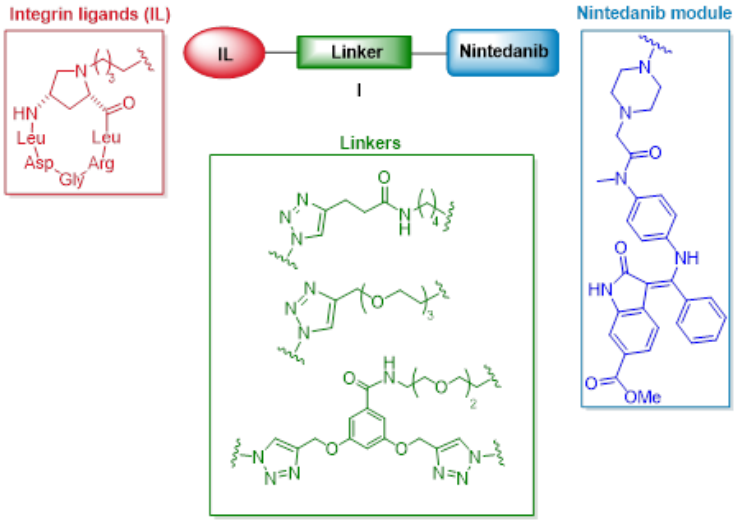
[b] Department of Experimental and Clinical Biomedical Sciences "Mario Serio", University of Florence, Viale Morgagni 50, 50134, Florence, Italy

E-mail: kelly.bugatti@unipr.it

ABSTRACT

Idiopathic Pulmonary Fibrosis (IPF) is a rare, chronic, and fibrotic lung disease, characterized by an extremely poor prognosis and a median survival after diagnosis around 3-5 years. Nowadays, the origin of IPF is not well known, but it is thought to be the result of aberrant wound-healing responses to repetitive lung injury. Nintedanib (a multi tyrosine-kinases inhibitor, TKI) is one of the two drugs currently approved for the treatment of IPF, although it just slows down the disease progression, while causing several off-target side-effects. For these reasons, research in the field of IPF is widely active, and many biological targets are currently under investigation, which may be considered selective biomarkers of the disease. [1]

The $\alpha_V\beta_6$ integrin has recently emerged as an attractive therapeutic target in the IPF treatment, mainly for two reasons: *(i)* this receptor is not expressed in healthy adult epithelia, but it is overexpressed in cancer and fibrosis; and *(ii)* the $\alpha_V\beta_6$ integrin activates the TGFβ cytokine, which is a central mediator of fibrogenesis, since it is upregulated in fibrotic diseases, and it mediates fibroblasts phenotype and function.



Based on this evidence and the promising results of previous work on integrin-based conjugates, [2] the aim of the present work was the construction of a panel of new conjugates covalently connecting an $\alpha_V\beta_6$ integrin-targeting ligand with the TKI nintedanib. In particular, three covalent conjugates of type **I** (see figure) were designed and synthesized, constituted by a nintedanib-like moiety as the TKI ingredient (depicted in blue), which is linked to an aminoproline-based cyclopeptide (depicted in red) [3] as selective $\alpha_V\beta_6$ integrin-targeting unit by means of three different robust triazole-based linkers (depicted in green).

The synthesized compounds were tested towards murine L929 fibroblasts. The selective cell internalization of the conjugates by $\alpha_V\beta_6$-mediated endocytosis was demonstrated, as well as inhibition of ERK phosphorylation and fibroblast-to-myofibroblast transition were proven, paving the way to novel investigations towards the development of potential selective antifibrotic drugs.

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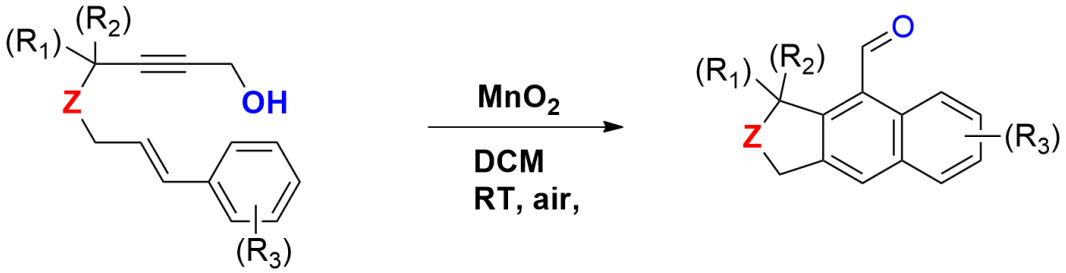
P13 – A MANGANESE-PROMOTED STEPWISE STYRYL-YNE DEAROMATIVE DIELS–ALDER CYCLIZATION FOR THE SYNTHESIS OF TRICYCLIC NAPHTHALENES

Nicola Camedda, Giovanni Maestri
Department SCVSA, University of Parma, Parco Area delle Scienze 17/A, 43124, Parma, Italy
E-mail: nicola.camedda@unipr.it

ABSTRACT

We would like to bring to your attention a poster featuring a catalytic dehydrogenative Diels-Alder reaction of styryl-ynols promoted by MnO_2. This method could be regarded as a convenient approach for the synthesis of a variety of naphthalene derivatives from the cheapest and most abundant source of manganese.
This approach affords products in moderate to excellent yield through the sequential oxidation of a propargyl alcohol, stepwise Diels–Alder cyclization, and finally rearomatization. The method displays a broad functional group tolerance, including halides, ethers, extended aromatic rings and heterocycles. The practical viability of the reaction is witnessed by its efficacy, which is retained up to a 1-mmol scale [1].



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P14 – RECOVERY BIOMASS TO REMOVE POLLUTANTS FROM WASTEWATER

Mirco Cescon, Tatiana Chenet, Giulia Vergine, Valentina Costa, Luisa Pasti
Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, via Luigi Borsari 46, 44121 Ferrara, Italy
E-mail: mirco.cescon@unife.it

ABSTRACT

Environmental pollution caused by heavy metals is one global problem leading to adverse effects on ecosystems, biodiversity and human health.
Among the most common physical and chemical approaches for the removal of heavy metals from water, adsorption is an effective and economic technique, offering flexibility in the design and operation, and a vast variety of adsorbent materials. In the last years, the use of natural or waste materials as adsorbents has been largely studied to favor eco-friendly approaches in environmental remediation applications. Among the waste products generated by food industry, mollusk shells have composition and structure characteristics suitable for the removal of heavy metals dissolved in water bodies. Indeed, many studies had reported the capability of molluscan and crustacean shell powder to adsorb heavy metals from water aqueous matrices.
In the present study, hydroxyapatite was synthetized from shells. Two synthesis approaches were employed to obtain hydroxyapatite, and these materials were characterized and their performances in the removal of cadmium from aqueous solutions were evaluated. The adsorbent material has been characterized by Thermogravimetric (TG) and X-ray diffractometric (XRD) techniques.
To investigate the kinetics and the thermodynamics of the adsorption process, adsorption measurements were carried at different concentration of cadmium. Inductively coupled plasma optical emission spectrometry (ICP-OES) was employed to determine cadmium concentration in the solution before and after the contact with the adsorbent materials. The results show high capacity towards the adsorption of this metal ion onto hydroxyapatite, moreover fast kinetics. The obtained results show that shells are a resource to prepare an eco-compatible adsorbent material which could be used for remediation technologies. Hydroxyapatite has been also investigated as support of a photocatalytic system, that is cadmium sulphide. Preliminary results are promising because it has been found that hydroxyapatite stabilizes the photocatalyst and limits the release of Cd^{2+} in solution during the photocatalytic process.

Figure 2. Shells of clams, oysters and other bivalve mollusks.

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P15 – FRAGMENT BASED AND APTAMER STRATEGIES TO DEVELOP RAD51-BRCA2 DISRUPTORS AND INDUCE SYNTHETIC LETHALITY

Andrea Ciamarone,[a,b] **Viola Previtali**,[a] **Jose Antonio Ortega Martinez**,[a] **Andrea Cavalli** [a,b]
[a] Computational and Chemical Biology, Istituto Italiano di Tecnologia, 16163 Genoa, Italy
[b] Department of Pharmacy and Biotechnology, University of Bologna, 40126 Bologna, Italy
E-mail: andrea.ciamarone@iit.it

ABSTRACT

Genomic instability is caused by an imbalance between DNA damage and DNA repair. Normal cells have very little DNA damage and have sufficient repair capacity to handle it. On the contrary, cancer cells suffer an excess of DNA damage and thus are sensitive to small perturbations in their DNA-repair capacity. In this context, synthetic lethality (SL) represents the key to selectively kill cancer cells while sparing normal cells. SL can be defined as the relationship that can occur between two genes where either one functioning maintains viability of the cell; however, upon dysfunction of both genes, the cell becomes unviable.[1] One well know example of synthetic lethality is the use of poly [ADPribose] polymerase (PARP) inhibitors (i.e. olaparib) in oncology patients with BRCA1/2 mutations. One of BRCA2's key roles is to recruit RAD51, an evolutionarily conserved recombinase involved in homologous recombination (HR) mechanism to repair double DNA strand breaks. Synthetic lethality arises from the simultaneous impairment of the repair mechanisms for single-strand and double-strand breaks.[2] Recent discoveries have shown how RAD51 is involved in a second synthetic lethality pair: RAD51/ Activation induced cytidine deaminase (AID). The latter is a DNA-directed cytidine deaminase that normally acts to initiate somatic hypermutation and immunoglobulin class switching in activated B-lymphocytes. Nevertheless, it was found that AID is often overexpressed in tumour cells in a range of cancer types. In this cells AID causes a high concentration of DNA double stranded breaks, leading to an obligate dependency on DNA break reapir for their duplication.[3] It is evident that the use of drugs able to bind RAD51 and inhibit HR represents a very promising method to combat cancer. To reach this result we will use two different strategies, One is based on the use of small molecules, while the other involves the use of aptamers. As regard the first, previous NMR fragment-based screening allowed to identify a fragment able to bind RAD51 and disrupts its interaction with BRCA2. Starting from these results, we aim to perform an extensive structure SAR study to transform this hit in a lead compound. (Figure 1) All the synthesized molecules will be evaluated through various biophysical assays. Cell viability and synergism assays in both the aforementioned synthetic lethality pathways (HR/PARP and HR/AID) will be further performed for the most promising structures. From a chemical point of view, the bi-cyclic heteroaromatic core allows to perform numerous disconnections designed to modify both one of the three portions, as well as a combination of them.

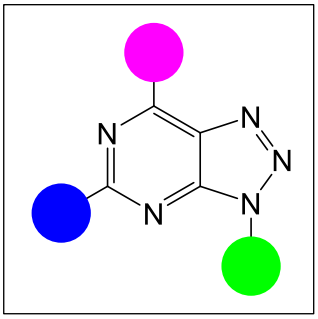

Figure 1. SAR studies will focus on 3 (green), 5 (blue) and 7 (pink) positions of initial fragment.

As regards the aptamer strategies, previous screening work has yielded some potential RNA aptamers of 12-15 bases able to bind RAD51, further studies will evaluate their ability to disrupt RAD51-BRCA2 protein-protein interaction. Starting from these results, we aim to introduce some chemical changes into their structure to make them more resistant to nucleases, increasing their *in vivo* half-life. If this new approach provides good results, aptamers could be used in different areas such as drug delivery and for diagnostic purposes.

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P16 – SIMULATING LIQUID CRYSTAL SELF-ASSEMBLY OF OLIGONUCLEOTIDES

Silvia Cristofaro, Silvia Orlandi, Luca Muccioli, Alberto Arcioni, Claudio Zannoni
Dipartimento di Chimica Industriale "Toso Montanari", Università di Bologna, viale del Risorgimento, 4, 40136 – Bologna (BO)
e-mail: silvia.cristofaro@unibo.it, s.orlandi@unibo.it, luca.muccioli@unibo.it, alberto.arcioni@unibo.it, claudio.zannoni@unibo.it;

ABSTRACT

Liquid crystals (LCs) are well-known functional soft materials, whose structures can be found in several biological molecules. LC ordering of DNA was first observed in vitro for long double strands, but only quite recently it started being considered as a common arrangement for DNA oligomers. Several examples have been described in the literature, such as sequence-directed self-assembly[1], base stacking driven structures[2] and various form of LC long-range ordering[3].
In this context, computer simulations could complement experiments with detailed insight into the processes involved in self-organization. We attempted to reproduce the LC ordering obtained from a solution of single strand GCCG oligonucleotides at relatively high saline concentration (in the range 0.6 M to 2.0 M), until now only experimentally observed by Bellini and coworkers[4]. By means of Molecular Dynamic simulations and through the usage of OxDNA[5] as coarse-grained model of representation for DNA interactions, we successfully demonstrated the lyotropic behavior of the GCCG oligonucleotide. Self-assembly for short strands is a consequence of pairing and staking interactions: oligomers rapidly hybridize into duplexes, which in turn organize themselves in linear aggregates. As the saline concentration is enhanced, linear aggregates align and form LC phases. Specifically, we found that oligomers undergo three main phase order transitions: isotropic to nematic, nematic to columnar and eventually from columnar to a surprisingly more disordered phase. LC phases attribution and characterization were performed by combining the quantitative assessment of orientational and positional order along with the diffusion coefficient calculation, which reveled to be functional to the understanding of the high concentration isotropic phase.

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P17 – ADDRESSING THE FRENKEL AND CHARGE TRANSFER CHARACTER OF EXCITON STATES WITH A DIMER-BASED MODEL HAMILTONIAN: APPLICATION TO LARGE AGGREGATES OF PERYLENE DIIMIDE

Yasi Dai,[a] Sofia Canola,[a,b] Giuseppe Bagnara,[a] Gaetano Ricci,[a,c] Fabrizia Negri [a,d]

[a] Università di Bologna, Dipartimento di Chimica 'Giacomo Ciamician', Via F. Selmi 2, 40126, Bologna, Italy

[b] Present address: Institute of Physics of the Czech Academy of Sciences, Cukrovarnická 10/112, CZ16200 Praha 6, Czech Republic

[c] Present address: Unité de Chimie Physique Téorique et Structurale & Laboratoire de Physique du Solide, Namur Institute of Structured Matter, Université de Namur, B-5000, Namur, Belgium

[d] INSTM, UdR Bologna, Via F. Selmi 2, 40126, Bologna, Italy

E-mail: yasi.dai2@unibo.it

ABSTRACT

The interchromophoric arrangements influence the intermolecular interactions inside an aggregate, which in turn, determine the unique optical properties, photo-induced processes and new functionalities of the aggregate. To mention just one example, the aggregate induced emission (AIE) [1], which consists in stronger fluorescence at aggregate level and finds applications in fluorescence detection of biomolecules and biomolecular processes. Generally, when talking about the excited states in aggregates, we always refer to exciton states. The nature of exciton states can generally be classified as Frenkel (FE)-dominated, charge-transfer (CT)-dominated or mixed CT/FE. The CT character has a crucial role in the photo-induced processes of an aggregate. [2–7] It is therefore fundamental to assess the CT/FE contributions to exciton states. Generally, from a quantum-chemical (QC) calculation, exciton states are expressed in terms of delocalized excitations (DEs). In order to extract the CT/FE character, we present a diabatization procedure with diabatic states chosen to coincide with local excitations within a restricted orbital space. On the other hand, a QC calculation will soon become unfeasible when considering very large aggregates. In this regard, we propose a model Hamiltonian (mH) approach built on the basis of QC calculations carried out only on dimers composing the aggregate [8]. Perylene Diimide (PDI) is chosen as a model system. Excitation energy profiles and CT/FE character modulations as a function of the interchromophore rearrangement are studied for aggregates of PDI up to tetramer. The dimer-based approach closely reproduces the results of full-aggregate calculations and the results demonstrate how the CT/FE interactions modulate the interchange of the H-/J- type aggregate for small longitudinal shifts of the chromophores.

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P18 – FIBER-REINFORCED CALCIUM PHOSPHATE CEMENT

M. F. Di Filippo,[a] D. Giuri,[a] C. Tomasini,[a] M. Maglio,[b] G. Marchiori,[b] S. Pagani,[b] M. Fini,[b] S. Panzavolta [a]

[a] Department of Chemistry, University of Bologna; E-mail: maria.difilippo5@unibo.it

[b] IRCCS Rizzoli Orthopedic Institute of Bologna

ABSTRACT

Calcium phosphate bone cements (CPCs) are biocompatible, bioactive and osteogenic systems which can be molded into bone defects and implant sites and then harden *in situ*, mimicking the mineral phase of native bone. However, their mechanical properties are far from those of bone, not only in terms of strength, but especially in terms of toughness, ductility and fatigue resistance.[1] The incorporation of fibers into a brittle cement matrix has been proven to increase the fracture toughness of the composite as well as the tensile and flexural strength by the crack arresting processes and it has been extensively explored even in the field of hydraulic cements and concretes for civil engineering and building applications.[1,2] Natural fibers and man-made fibers have been used for this purpose [1], but, on the best of our knowledge, they have always been introduced inside the pasty material after their synthesis. In order to obtain a better cohesion between fibers and cement paste thus improving the mechanical performances, in this work we demonstrate the feasibility of forming self-assembling fibers in just one step during cement setting. Fibers were obtained by the introduction of a low-molecular-weight gelator (MW < 1000 Da) able to form supramolecular structures stabilized by weak interactions. Addition of proper amount of Ca^{2+} ions promotes fibers assembling inside the cement paste thus producing a composite matrix where the fibers are strictly embedded.[3] Our gelator is composed of Boc-L-Dopa(OBn)$_2$-OH, which chelates Ca^{2+} ions in order to arrange in fibers. The cement powders are composed of a gelatin/α-TCP mix and $CaHPO_4 \cdot 2H_2O$, while the liquid phase is made by an aqueous solution of the gelator at two different concentrations: 2 and 5% wt. $CaCl_2$ was added as a trigger to the gelator solution, which was mixed with the cement powders to obtain a paste of workable consistency. Barium sulfate was added to the cement composition as radiopacifying agent. Mechanical properties under compression and flexural properties were evaluated, as well as porosity studies by means of MicroCT. Rheological measurements and morphological investigations by means of SEM were also performed. The compositions were optimized in order to obtain injectable cements. Eventually, in vitro biocompatibility with osteoblast-like cells MG63 and qPCR gene expression were performed to ensure the biocompatibily of the materials.

Mechanical tests confirmed that the gelator addition to the cements is able to enhance their mechanical strength, especially when tested in bending, and to increase their work of fracture. MicroCT analyses showed no significant variation in the porosity of the composite materials. Moreover, biological assays ensured the biocompatibility of the materials and their ability to express the main gene markers that are necessary for bone formation.

The approach used in this work could represents a new, simple and effective method to obtain cements reinforced with self-assembled fibers in just a single step. The formation of fibers during the hardening reaction provides structural and mechanical support to the material without interfering with their porosity. The obtained fiber-reinforced CPC is biocompatible and able to promote the deposition of extracellular matrix.

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P19 – DEVELOPMENT AND FORMULATION OF NATURALLY DERIVED BIOINKS FOR 3D BIOPRINTING APPLICATION

L. Di Lisa,[a] G. Pagnotta,[a] R. Spigarelli,[b] C. Valerii,[b] E. Spisni,[b] M. L. Focarete [a]
[a] Department of Chemistry "G. Ciamician", University of Bologna, Bologna, Italy
[b] Department of Biological, Geological, and Environmental Sciences, University of Bologna, Bologna, Italy
Email: luana.dilisa@studio.unibo.it

ABSTRACT

3D bioprinting is a powerful technology that allows the fabrication of complex 3D constructs, through the precise deposition of bioinks in a layer-by-layer manner, which represent the physiologically-like human ECM. Bioinks are composed of a polymeric part (hydrogels) [1] and a cellular part. Bioinks should display some characteristics including (i) excellent printability, (ii) high mechanical integrity, (iii) biocompatibility, and (iv) non-toxicity. In the last twenty years, 3D bioprinting had a great impact on applications in the biomedical field, since it allows to reproduce 3D models, which can be applied in tissue engineering and drug screening. In this work, gelatin methacrylate (GelMa), collagen and IPN of GelMa and collagen bioinks, classified as the most biocompatible and bioactive matrices, were developed.

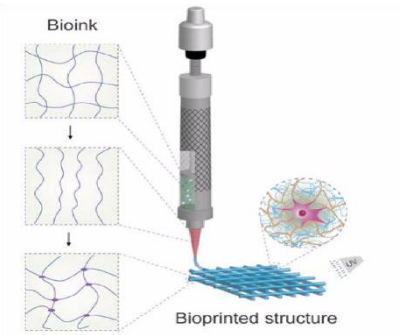

Fig.1 Schematic illustration of the 3D Bioprinting process

The synthesis of GelMa was carried out by following a gelatin methacrylation process [2]. Pure collagen formulation was optimized in collaboration with Typeone biomaterials s.r.l. The IPN was produced to both exploit the tunable mechanical properties of the GelMa and the excellent biological and chemical properties of the collagen. To better understand which were the most performing formulations in terms of mechanical and biological properties, various parameters were evaluated, such as (i) hydrogels concentration (ii) photoinitiator (Irgacure 2959) concentration, (iii) intensity and time exposure of UV light for the crosslinking process. A rheological characterization was performed on the optimized bioinks formulation containing CaCo-2 cell line (used to reproduce the epithelial monolayer of the intestine), to correlate their rheological properties with the bioprinting process. A morphological (SEM) analysis was performed to characterize the porosity of the 3D constructs. Finally, cell viability and immunohistochemical analysis were performed to assess cell viability, adhesion and cell proliferation. Rheological results showed that IPN displays intermediate rheological properties, better tunable stiffness and higher ability to recover its mechanical properties with respect to the single components. The morphological analysis showed that by tuning the matrix cross-linking degree, it is possible to fine tune the matrix porosity, which is useful for ensuring cell proliferation and nutrition. The biological tests confirmed high cell viability inside all the matrices, even after photo-crosslinking, and the successful formation of the intestinal epithelial monolayer especially within the collagen-based bioinks.

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P20 – DISCOVERY OF NOVEL SPIROCYCLIC COMPOUNDS FOR THE TREATMENT OF MYOCARDIAL REPERFUSION INJURY

M. Fabbri,[a] **G. Morciano**,[b] **G. Pedriale**,[c] **V. Albanese**,[a] **S. Pacifico**,[a] **S. Missiroli**,[b] **R. Ferrari**,[c] **G. Campo**,[c] **C. Giorgi**,[b] **P. Pinton**,[b] **R. Guerrini**,[a] **C. Trapella**,[a] **D. Preti** [a]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Ferrara, Italy

[b] Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, Ferrara, Italy

[c] Maria Cecilia Hospital GVM Care & Research, Ravenna, Italy and Cardiovascular Institute Azienda Ospedaliera-Universitaria S. Anna, Ferrara, Italy

ABSTRACT

Acute myocardial infarction (MI) is one of the leading causes of death and disability worldwide and reperfusion injury (RI) is known to contribute for up to the 50% of the final infarct size. Rising data indicate that the onset of RI involves several molecular and cellular factors that culminate in the final opening of a large pore in the mitochondrial membrane, namely the mitochondrial permeability transition pore (mPTP).[1] mPTP is recognized as the key actor in the final step of RI and the main responsible for cardiomyocyte death, which makes it a major therapeutic target for cardioprotection. The incomplete knowledge of the bio architecture of mPTP is the main obstacle in drug discovery programs, however recent findings suggest that mPTP would reside in the c-ring of F_1F_O-ATP synthase.[2] Our research group supported this evidence reporting the discovery of the first small-molecule inhibitors of mPTP that target the c subunit of F_1/F_O-ATP synthase.[3] **PP11**, the parent compound of the series, was designed from the structure of Oligomycin A, a known c ring ligand (Fig. 1). The following SAR optimization led to **IB13** which showed beneficial effects in an ex vivo model of MI.[3] Based on these preliminary results we focused on the design and synthesis of isatin-based spirocycles with the general structure **MF**, in order to identify novel clinically useful mPTP inhibitors (unpublished). The synthesized molecules were tested in vitro, and all these novel spiro-derivatives demonstrated to inhibit mPTP opening. Specifically, compound **MF16** (Fig. 1) is the most promising compound of the series, with an 83% inhibition at 1µM concentration. Despite these important results, the exact binding site of these molecules at the target protein is still unknown. Thus, we designed and synthetized photoaffinity probes (PAPs) as tools to employ in binding site deconvolution studies. Photoaffinity labeling (PAL) is a validated methodology in drug discovery for probing the position and coordinates of ligand binding sites.[4] We firstly designed PAPs using the acquired SAR information on **PP11** which guided us to incorporate a photoactivating group and a terminal alkyne click handle in strategical positions without altering the biological activity (Fig. 1).

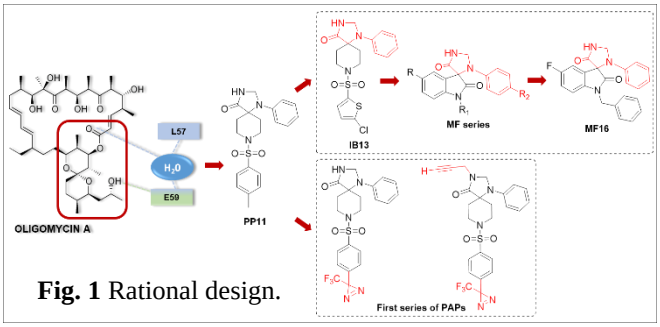

Fig. 1 Rational design.

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P21 – DESIGN AND SYNTHESIS OF RAD51-BRCA DISRUPTORS TO INHIBIT HOMOLOGOUS RECOMBINATION AND ACHIEVE SYNTHETIC LETHALITY IN CANCER CELLS

Giovanni Ferrandi,[a,b] **Marinella Roberti**,[a] **Andrea Cavalli** [a,b]
[a] Department of Pharmacy and Biotechnology, University of Bologna, Via Belmeloro 6, 40126, Bologna, Italy
[b] Computational & Chemical Biology, Istituto Italiano di Tecnologia, Via Morego 30, 16163, Genova, Italy
E-mail: giovanni.ferrandi2@unibo.it

ABSTRACT

My research aims at synthetizing and optimizing small molecules able to disrupt RAD51-BRCA protein-protein interaction and trigger synthetic lethality (SL) in cancer cells, in combination with poly [ADP-ribose] polymerase (PARP) inhibitors.
SL is phenotypic condition in which the cell does not survive due to the combination of two specific genetic perturbations, which taken individually do not induce cell death. One example of SL is the use of the PARP inhibitor Olaparib in oncology patients with BRCA mutations. PARP is involved in the repair of single-strand breaks (SSBs), whereas BRCA2 is essential for repairing DNA double-strand breaks (DSBs) by homologous recombination (HR) as it recruits RAD51 from the cytosol.
In this context, the group on which I will carry out my PhD thesis recently exploited a new drug discovery paradigm, triggering fully small-molecules-induced SL by combining RAD51-BRCA2 disruptors with Olaparib to target pancreatic cancer (Fig. 1). The objective is to widen the use of $PARP_i$ in BRCA-competent and Olaparib resistant cancer. Moreover, the overexpression of RAD51 is elevated in a wide variety of cancers and correlated with resistance to radio- or chemotherapy that induces DNA damage. Therefore, targeting RAD51-BRCA2 interaction allows overcoming resistance of cancer cells to existing DNA-damaging therapies.[2]
My first-year PhD project aims to synthetize and optimize analogs of a quinoline-based RAD51-BRCA disruptor identified as a promising hit compound through a virtual screening (VS) campaign (Fig. 1). Using a *hit to lead* strategy, I will carry out SAR studies around the most promising derivatives. An innovative aspect of this project will be the use of an interactive in silico platform, supported by artificial intelligence (AI), for the retrosynthetic study of the final products.[3] This tool allows to select the best reagents and conditions, thus reducing time for planning reactions and enabling a decrease in waste, consistently with the green chemistry approach informing my research.

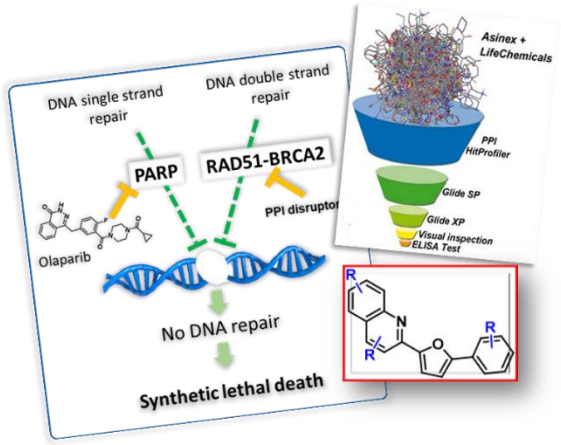

Figure 3. Synthetic lethality scheme (left), VS on RAD51 and hit compound to SAR study (right)

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P22 – EFFECTS OF *MORINGA OLEIFERA* LEAF EXTRACTS ON *XANTHOMONAS CAMPESTRIS PV. CAMPESTRIS*

Riccardo Fontana,[a,b] Anna Caproni,[a] Raissa Buzzi,[b] Mariaconcetta Sicurella,[a] Mattia Buratto,[a] Francesca Salvatori,[a] Mariangela Pappadà,[a] Stefano Manfredini,[b] Anna Baldisserotto,[b] Peggy Marconi [b]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, 44121 Ferrara, Italy

fntrcr1@unife.it (R.F.); anna.caproni@edu.unife.it (A.C.); mariaconcetta.sicurella@unife.it (M.S.); mattia.buratto@unife.it (M.B.); francesca.salvatori@unife.it (F.S.); mariangela.pappada@unife.it (M.P.); peggy.marconi@unife.it (P.M.)

[b] Department of Life Sciences and Biotechnology, University of Ferrara, 44121 Ferrara, Italy

raissa.buzzi@unife.it (R.B.); anna.baldisserotto@unife.it (A.B.); stefano.manfredini@unife.it (S.M.)

ABSTRACT

Xanthomonas campestris pv. *campestris* (Xcc) is a Gram-negative bacterium belonging to the Xanthomonodaceae family, causing black rot in crucifers. To control this pathogen, the study investigated the effect of different leaves extracts of *Moringa oleifera* Lam., a tropical plant, well known for its food properties and with countless applications in many different fields, from nutraceutical (hypoglycemic) to the cosmetic (sunscreen) properties. Nevertheless, several studies pointed to its antibacterial action against both Gram-negative and Gram-positive bacteria. Many bioactive compounds, including flavonoids, phenolic acids, alkaloids, isothiocyanates, tannins and saponins, contained in these extracts, were found responsible for its countless activities. The analyses carried out in this study showed that the *M. oleifera* Lam. Methanolic (MeOH-MOE), hydroalcoholic (HA-MOE) and hydroalcoholic with maltodextrin (HAMD-MOE) extracts had both bacteriostatic and bactericidal effects at concentrations of 0.5, 0.5 and 0.1 mg/mL respectively. In particular, the study showed how all extracts were able to alter membrane permeability, to adversely affect swarming motility, and to alter biofilm formation in Xcc. The most present active ingredients were found to be ferulic acid, rutin and chlorogenic acid. HA-MOE was in fact the extract that showed the highest concentration of polyphenols, presenting an excellent percentage of rutin and ferulic acid, and great results in all performed experiments. HA-MOE, HAMD-MOE and MeOH-MOE were found comparable in terms of activity and in terms of polyphenol percentage, but the highest effect of the HAMD-MOE extract was probably due to the maltodextrins themselves which are generally added as processing aids in spray drying processes, as they act as coating agents incorporating bioactive molecules, prolonging shelf life and preventing loss of activity. The in-planta experiments showed a reduction of the necrosis area in the infected radishes, although the ability of the extracts to be absorbed by root systems, in order to reach the target point, is yet to be understood.

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P23 – SYNERGIC ACTIVITY OF LIGNIN AND COPPER FOR A MORE SUSTAINABLE AGRICULTURE

Cristina Gazzurelli,[a] Dominga Rogolino,[a] Mauro Carcelli,[a] Giuliano Leonardi,[b] Suvi Pietarinen,[c] Andrea Migliori,[d] Paolo Pelagatti [a]

[a] Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/A, Parma, 43124, Italy; E-mail: cristina.gazzurelli@unipr.it

[b] Green Innovation GMBH, Grabenweg 68, Innsbruck, 6020, Austria

[c] UPM-Kymmene Oyj, Alvar Aallon katu 1, Helsinki, FI-00101, Finland

[d] CNR-IMM, Sezione di Bologna, via Gobetti 101, Bologna, 40129, Italy

ABSTRACT

After cellulose, lignin is the most abundant plant derived polymer. Its role in plants is to confer mechanical support and to protect against pests and diseases. This is possible thanks to its polyphenolic structure that imparts antibacterial, antifungal and antioxidant properties to the polymer [1]. About 70 million tons per year of lignin are obtained from several industrial processes, 60% being treated as a waste, while the remaining 40% is burnt to get energy with the unwanted production of CO_2 [2]. Scientific research is working to find potential applications for lignin [3] in the field of functional materials, as precursor for small molecules by depolymerization, as well as in the packaging field [1,2].

In the agricultural field, the use of copper as pesticide is an increasing problem. Nowadays, copper-based pesticides are still extensively used owing to their efficacy, but problems related to its accumulation into the soil and groundwater contamination require research to find alternatives [4].

It is in this scenario that the project of my PhD takes place. The idea is to develop new environmentally benign pesticides exploiting the synergy deriving from the combination of lignin with copper [5]. Starting from lignin and Cu_4SO_4, two different hybrid materials were synthesized under different experimental conditions, named lignin@brochantite (brochantite = $Cu_4(SO_4)(OH)_6$) [5], and lignin@cuprite, (cuprite = Cu_2O), Figure 1. XRPD and TEM analysis revealed the formation of hybrid materials in which nanocrystals of the respective mineral phases were embedded in the lignin matrix. The characterization of the materials was based on XRPD, ICP, TEM, GPC, Py-GC/MS, NMR and IR analysis, to determine the nature and features of the crystalline phases (copper content, morphology and dimension of the crystals) as well as the intactness of the biopolymer. The antibacterial activity of these new hybrid materials was evaluated against several pathogens by *in vitro* and *in vivo* tests on tomato plants. These trials revealed a high efficiency with a lower amount of copper compared to copper-based pesticides currently on the market. The synergistic effect between copper and lignin was thus confirmed [5,6]. A correlation between the morphology of the crystals and their effectiveness with *in vivo* tests was also conducted [6].

Figure 1. TEM image of crystals of brochantite contained in lignin@brochantite.

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P24 – SYNTHESIS AND CATALYTIC ACTIVITY OF CALIX[6]ARENE-BASED GOLD(I) CAVITANDS

Gabriele Giovanardi, Andrea Secchi, Arturo Arduini, Gianpiero Cera
Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco Area delle Scienze 17/A, 43124 Parma, Italy
E-mail: gabriele.giovanardi@unipr.it

ABSTRACT

An important goal that has been tackled in supramolecular chemistry is the synthesis of multifunctional organometallic macrocycles for catalysis. Cutting-edge contributions demostrated the ability of calix[n]arene[1] and resorcinarene-based[2] cavitands, appropriately functionalized with phosphine ligands, to promote highly selective metal-catalyzed transformations. We report the synthesis and characterization of a novel phosphine calix[6]arene ligand **A** (Figure 1).

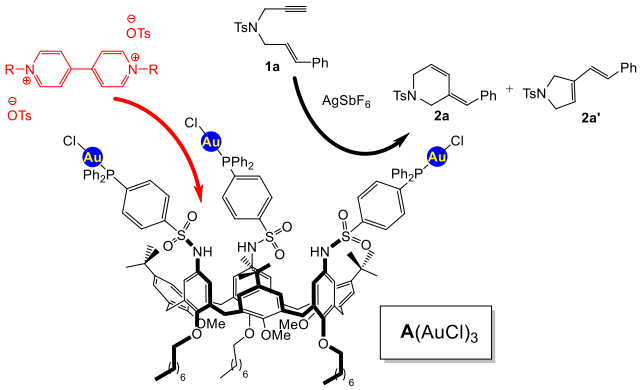

Figure 1. Triphoscalix[6]arene gold(I) macrocycle for molecular recognition and catalysis.

This supramolecular wheel, with recognition features governed by the sulfonamido hydrogen-bonding domain, was exploited to synthetize multitasking gold(I) complexes, used for the synthesis of interwoven (pseudo)rotaxane species and for catalytic cycloisomerization reaction of 1,6-enynes.[3] We first evaluated the ability of **A**$(AuCl)_3$ to work as supramolecular receptors for dialkyl viologen salt (DOV·2TsO). NMR analysis shown the formation of a pseudorotaxane complex where the trisulfonamide calix[6]arene scaffold adopt a *partial cone* conformation. Successively, we investigated the reactivity of the novel **A**$(AuCl)_3$ complex in catalytic cycloisomerization of 1,6-enyne **1a**. We observed a quite remarkable selectivity (14:1) toward the formation of the 6-endo-dig rearranged diene **2a** with respect to **2a'**, formed by an initial 5-exo-deg cyclization, instead. The role of the calix[6]arene scaffold was studied by running the catalytic reaction with a monomeric sulfonamide-based gold(I) analogue and in the presence of a competitive binder. In the first case we observed a slight drop in regioselectivity (**2a**/**2a'** = 12:1) that highlighted the cooperative role of the three phosphines in the calix[6]arene ligand in controlling the selectivity of the reaction. Contrarily, the reaction conducted with DOV·2TsO as additive did not display any substantial variation, suggesting that the catalytic event occurs outside of the cavity. Further analysis are required to investigate the role of the calix[6]arene scaffold in determining the regioselectivity of the catalytic reaction.

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P25 – MOLECULAR SENSITIZERS FOR PHOTO-3D PRINTING OF CERAMIC COMPONENTS

Silvia Grandi,[a] Stefano Caramori,[a] Edoardo Marchini,[a] Francesca Mazzanti,[b] Enrico Leoni [b]
[a] Università di Ferrara, Dipartimento di Scienze Chimiche, Farmaceutiche ed Agrarie, via Luigi Borsari 46, 44121 FE
[b] ENEA, Laboratorio Tecnologie dei Materiali di Faenza, via Ravegnana 186, 48018 RA
E-mail: grnslv@unife.it

ABSTRACT

In recent years there's been a growing interest in additive manufacturing and 3D printing. These techniques can be applied to different technological fields and, in particular, they can be proposed as one of the possible solutions to ceramic materials' processing. Ceramics are characterized by high hardness, chemical stability and high-temperature resistance. They are also biocompatible and suitable for the realization of different kind of implants, prostheses and biomedical devices.[1] Through the application of additive manufacturing technologies to ceramic materials, it is possible to obtain three-dimensional structures with high degree of accuracy and high surface finish, that couldn't be obtained otherwise with conventional machining.

In this work we have studied particular compositions of photopolymeric resins added with ceramic powders, which can be used in the 3D printing technique known as Digital Light Processing, suitable for the manufacturing of complex geometry products with high degree of detail.[2]

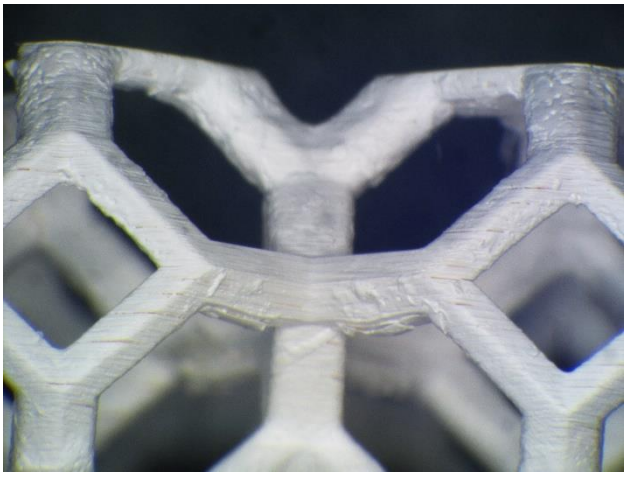

Figure 1. 3D printed ceramic object based on zirconia and yttria, obtained by vat polymerization triggered by visible light.

The term '3D printing' indicates the building up process of three-dimensional structures from a digital file. The object is created by laying down successive layers of material in order to obtain a complete solid. The technique we employed is called vat polymerization, that involves a photopolymerization of a liquid monomeric resin. We have selected three different visible light absorbers (sensitizers), acting as photoinitiators towards photopolymerization.[3]

After gaining mechanistic information about the electron transfer events which trigger visible light photopolymerization we have formulated resins that were tested and validated in the 3D printing process of ceramic materials.

This work has demonstrated the pivotal role of the sensitizers in determining the rate of the photolopymerization that is a critical parameter for achieving a good precision and definition in the photo-3D printing of ceramic objects with complex geometry.

This process could be further optimized through some modifications of the molecular structure of common organic sensitizers, allowing to reach higher quality in the production of ceramic objects for biomedical applications.

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P26 – EXPANDING THE TOOLBOX OF HETEROGENEOUS ASYMMETRIC ORGANOCATALYSTS: BIFUNCTIONAL CYCLOPROPENIMINE SUPERBASES FOR ENANTIOSELECTIVE CATALYSIS IN BATCH AND CONTINUOUS-FLOW

Costanza Leonardi,[a] Arianna Brandolese,[a] Lorenzo Preti,[a] Lorenzo Poletti,[a] Olga Bortolini,[a] Eleonora Polo,[b] Paolo Dambruoso,[b] Daniele Ragno,[a] Graziano Di Carmine,[a] Alessandro Massi [a]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via L. Borsari, 46, 44121 Ferrara, Italy

[b] Istituto per la Sintesi Organica e la Fotoreattività, Consiglio Nazionale delle Ricerche, Via P. Gobetti, 101-40129 Bologna, Italy

ABSTRACT

In recent years, chiral cyclopropenimines have been coming to light as effective Brønsted base orgacatalysts in enantioselective reactions by HOMO activation of pronucleophiles with high pKa values [1].

However, due to their inherent strong reactivity, cyclopropenimines are difficult to access in terms of preparation and purification. In this direction, organocatalyst heterogenization offers unique opportunities by facilitating the catalyst handling, recycling, and easy product/catalyst separation.

In this context, we describe an unprecedented strategy for the immobilization onto polystyrene and silica supports of chiral 2,3-bisaminocyclopropenimine, which is a privileged bifunctional organocatalyst for highly enantioselective Michael reactions [2].

The activity and recyclability of polystyrene- and silica-supported cyclopropenimines were initially tested under batch conditions in a model Michael addition detecting comparable efficiencies but a superior stability of the latter heterogeneous catalyst (5 cycles, accumulated TON of 27.1).

The preferred silica-supported cyclopropenimine behaved very similarly to the soluble counterpart in the reaction of glycine imine with different Michael acceptors (48-92% yield; 60-98% ee) and it could be utilized for the first time as packing material for the fabrication of fixed-bed mesoreactors (pressure-resistant stainless-steel columns). Continuous-flow experiments were performed with satisfactory long-term stability (24 h on stream) with unaltered conversion efficiency and enantioselectivity.

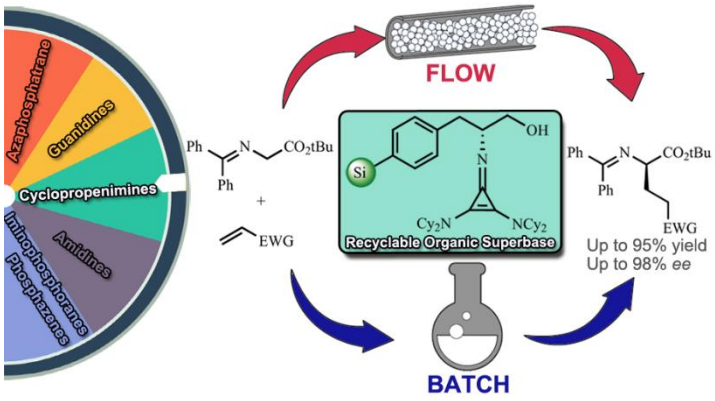

Figure 4: Supported cyclopropenimine catalyst in model Michael reaction in heterogeneous phase.

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P27 – LITHIUM–OXYGEN BATTERY EXPLOITING HIGHLY CONCENTRATED GLYME-BASED ELECTROLYTES

Stanislav Levchenko,[a] Vittorio Marangon,[a] Celia Hernandez-Rentero,[b] Giacomo Bianchini,[a] Davide Spagnolo,[a] Alvaro Caballero,[b] Julian Morales,[b] Jusef Hassoun [a]

[a] Department of Chemical and Pharmaceutical Sciences, University of Ferrara, 44121, Ferrara, Italy

[b] Dpto. Química Inorgánica e Ingeniería Química, Instituto de Química Fina y Nanoquímica, Universidad de Córdoba, 14071 Córdoba, Spain

ABSTRACT

Concentrated solutions of lithium bis(trifluoromethanesulfonyl)imide (LiTFSI) and lithium nitrate ($LiNO_3$) salts in either diethylene-glycol dimethyl-ether (DEGDME) or triethylene-glycol dimethyl-ether (TREGDME) are herein characterized in terms of chemical and electrochemical properties in view of possible applications as the electrolyte in lithium–oxygen batteries. X-ray photoelectron spectroscopy at the lithium metal surface upon prolonged storage in lithium cells reveals the complex composition and nature of the solid electrolyte interphase (SEI) formed through the reduction of the solutions, while thermogravimetric analysis shows a stability depending on the glyme chain length. The applicability of the solutions in the lithium metal cell is investigated by means of electrochemical impedance spectroscopy (EIS), chronoamperometry, galvanostatic cycling, and voltammetry, which reveal high conductivity and lithium transference number as well as a wide electrochemical stability window of both electrolytes. However, a challenging issue ascribed to the more pronounced evaporation of the electrolyte based on DEGDME with respect to TREGDME actually limits the application of the former in the Li/O_2 battery. Hence, EIS measurements reveal a very fast increase in the impedance of cells using the DEGDME-based electrolyte upon prolonged exposure to the oxygen atmosphere, which leads to a performance decay of the corresponding Li/O_2 battery. Instead, cells using the TREGDME-based electrolyte reveal remarkable interphase stability and much more enhanced response with specific capacity ranging from 500 to 1000 mA h g^{-1} referred to the carbon mass in the positive electrode, with an associated maximum practical energy density of 450 W h kg^{-1}. These results suggest the glyme volatility as a determining factor for allowing the use of the electrolyte media in a Li/O_2 cell. Therefore, electrolytes using a glyme with sufficiently high boiling point, such as TREGDME, which is further increased by the relevant presence of salts including a lithium protecting sacrificial one ($LiNO_3$), can allow the application of the solutions in a safe and high-performance lithium–oxygen battery.[1]

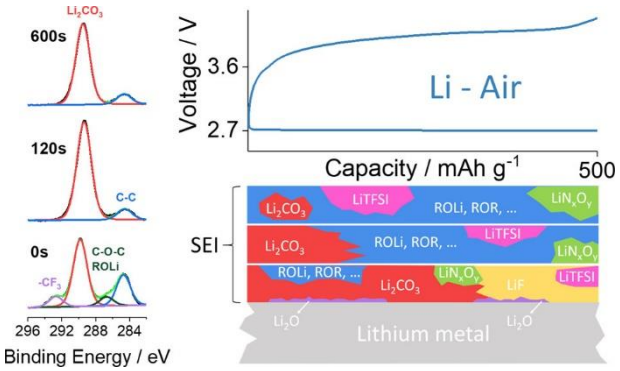

Figure 5. At the left deconvoluted XPS spectra of C 1s for DEGDME-based electrolyte. At the top right voltage profile of the first cycle of the lithium-oxygen cell employing TREGDME-based electrolyte. At the bottom right scheme of the SEI layer on the lithium metal anode.

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P28 – ELECTROCHEMICAL STUDY OF TITANIUM HEXACYANOFERRATE IN ORGANIC AND AQUEOUS BATTERIES

Min Li,[a] Mariam Maisuradze,[a] Alessandro Bina,[a] Angelo Mullaliu,[b,c] Stefano Passerini,[b,c] Marco Giorgetti [a]

[a] Department of Industrial Chemistry "Toso Montanari", University of Bologna, Viale Risorgimento 4,40136 Bologna, Italy

[b] Helmholtz Institute Ulm (HIU), Helmholtzstrasse 11, 89081 Ulm, Germany

[c] Karlsruhe Institute of Technology (KIT), P.O. Box 3640, 76021 Karlsruhe, Germany

ABSTRACT

Titanium Hexacyanoferrates (TiHCF), as prussian blue analogue, was synthesized by simple co-precipitation method, with unit of -Fe-CN-Ti-, and its electrochemical performance was studied in organic Li-ion and Na-ion batteries [1,2]. The result demonstrates that TiHCF is a good cathode material for both Li-ion and Na-ion batteries. Compared to Li-ion battery, TiHCF shows better electrochemical performance as a Na-ion host, offering a capacity of 74 mAh g^{-1} at C/20 and 94.5% retention after 50 cycles. This is due to the activation of Ti sites towards the redox reaction, making TiHCF a good candidate electrode material for Na-ion battery [3]. Meanwhile, the two well-separated redox peaks ($Fe^{3+/2+}$ and $Ti^{4+/3+}$) enable TiHCF can be used as electrode material for symmetric batteries. And for the first time, TiHCF was used as both cathode and anode for aqueous Na-ion, K-ion and Mg-ion symmetric batteries. The result shows that all the symmetric batteries exhibit a voltage plateau centered at around 0.6 V, with discharge capacity around 30~40 mAhg^{-1} at C/5. The calculated diffusion coefficient of Na^+, K^+ and Mg^{2+} are in the same order of magnitude, which indicates that the three-dimensional ionic channels and interstices in the lattice of TiHCF are large enough for an efficient Na^+, K^+ and Mg^{2+} insertion and extraction. The advantages of aqueous symmetric batteries with high safety and low cost may provide a solution for large-scale stationary energy storage, even considering the low intrinsic specific capacity these systems display.

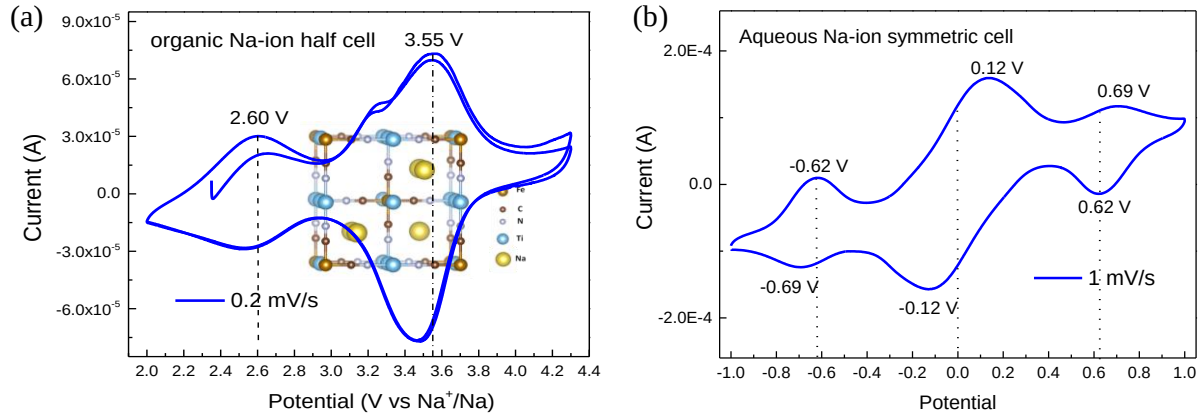

Figure 1 (a) Cyclic voltammetry (CV) of TiHCF Na-ion half cell at 0.2 mV/s at the potential range 2.0~4.2 V ; (b) CV of TiHCF aqueous Na-ion full cell at 1 mV/s at the potential range -1.0~1 V.

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P29 – STABILIZER'S EFFECT ON Au NANOPARTICLES ACTIVITY FOR THE SELECTIVE OXIDATION OF HMF

Francesca Liuzzi, Alessandro Allegri, Stefano Scurti, Nikolaos Dimitratos, Daniele Caretti, Stefania Albonetti
Department of Industrial Chemistry "Toso Montanari", University of Bologna, Viale Risorgimento 4, 40136 Bologna, Italy; E-mail: stefania.albonetti@unibo.it

ABSTRACT

5-Hydroxymethylfurfural (HMF) is generally accepted to be one of the most versatile compound derived from biomasses. From its oxidation, it is possible to produce 2,5-furandicarboxylic acid, (FDCA) which is a possible biomass-derived substitute for terephthalic acid. Gold nanoparticles-based catalysts have been found to be very active in this oxidation. In particular, the activity of these materials is correlated with the dimensions of Au: smaller nanoparticles lead to more active catalysts.[1] Sol-immobilization is a technique that, unlike many others, allows the use of stabilising agents to control particle size. However, when these catalysts are employed without a pre-treatment to remove the stabilizer, its presence on the surface of nanoparticles can greatly influence the catalytic activity, modifying the interactions between reagents and active phase.[2] Several works have shown how removing the stabilizer influences the catalytic performances, but only few have paid attention on the effect which these molecules have on the catalytic properties. The purpose of this work is to study the effect of some polymeric stabilizers on the activity of gold nanoparticles. In particular, some gold-based catalysts, prepared via sol-immobilization and supported on active carbon, (Au/AC) were tested in the selective oxidation of HMF to FDCA. First of all, three commercial polymers (PVP, PEG and PVA) were employed in the synthesis of Au/AC catalysts to study the influence of the stabilizer on the catalytic performances. This study has highlighted a double effect of the capping ligand: its presence allows to obtain smaller and more active nanoparticles, but, at the same time, it becomes a diffusive barrier for the reagents and modifies the catalysts activity. Since catalysts with PVA as stabilizer have shown better performances, two similar polymers (polyvinylamine and phosphorylated polyvinylalcohol), with different functional groups, have been synthesised, in order to study how different electronic effects can condition the catalytic activity. Interesting results have been achieved with the polyvinylamine as stabilizer, in fact, its nature of strong electron-donor affects the catalyst activity leading to a change in the mechanism pathway (Figure 1).

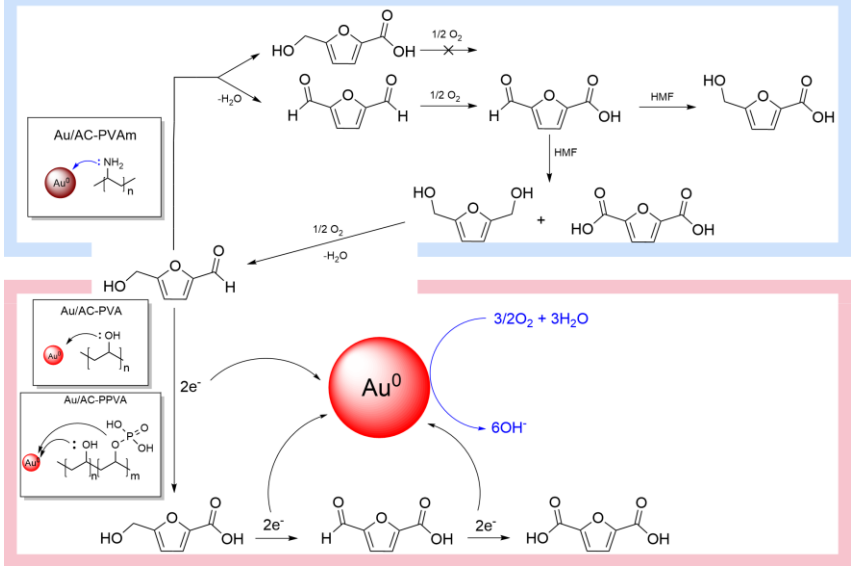

Figure 6: Different reaction pathways on different Au/AC catalysts

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P30 – POLLUTION AND EXPOSOME: SEARCH FOR BIOMARKERS OF EFFECT

Chiara Maccari, Roberta Andreoli
Laboratory of Industrial Toxicology and Advanced Analytical Methods, Department of Medicine and Surgery, University of Parma
E-mail: chiara.maccari@unipr.it

ABSTRACT

Environmental air pollutants are a complex mixture of toxics that, even if present at relative low concentrations, have a negative impact on public health. Together with lifestyle, eating habits, and occupational exposure, they contribute to create an inflammatory status and oxidative stress both in healthy subjects than in patients; moreover, many of these factors are difficult to control or eliminate by the subject himself. Thus, it's important to identify specific biomarkers usefully to characterize the individual factors that generate oxidative stress and, above all, to identify which types of subjects are most at risk.
The possibility to define the different contributions of exposure to environmental contaminants (biomarkers od exposure) and its effects in terms of oxidative stress (biomarkers of effects) would allow to create a more complete description of the healthy status of general population and could be used both at the stage of prevention and early detection of diseases.
Numerous studies agree on the need to study the general population by identifying "reference" exposure values [1] in order to use, in the future, the assay of these biomarkers for early diagnostic purposes.
For both types of biomarkers, of exposure and of effect, it is necessary to deepen the mechanisms of action with which they are produced, their metabolism and the role that they play in the different pathologies; in order to try to predict their effects on the health of the general population.[2].
Quantifying these biomarkers in the urine would allow to better describe how pollution should be associated with oxidative damage and hypo-methylation of DNA, resulting in genome instability. Moreover, the possibility to quantify both biomarkers of exposure and of effect in matrices other than urine, such as hair, saliva or exhaled breath condensate could better explain the different mechanisms of action of pollutants and of oxidative stress, in terms of concentration, sampling time, and biological meaning. [3]. The choice to sample accessible biological matrices also allow to investigate the biomarkers in children, in fragile subjects, or to plan repeated measurements studies on cohorts of healthy subjects. The goal of this project is to identify a package of biomarkers of exposure to environmental pollutants and of biomarkers of effect related to oxidative stress, able to characterize the correlation between pollutions and oxidative damage and to describe the state health of both the general population and patients with inflammatory diseases.

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P31 – USING TXM AND 2D-XRF FOR THE IDENTIFICATION OF INHOMOGENEOUS STATE OF CHARGE IN MANGANESE HEXACYANOFERRATE CATHODE MATERIAL

Mariam Maisuradze,[a] Min Li,[a] Angelo Mullaliu,[b,c] Andrea Sorrentino,[d] Dino Tonti,[e] Ilaria Carlomagno,[f] Giuliana Aquilanti,[f] Jasper Rikkert Plaisier,[f] Stefano Passerini,[b,c] Marco Giorgetti [a]

[a] Department of Industrial Chemistry "Toso Montanari", University of Bologna, Viale del Risorgimento 4, 40136 Bologna, Italy; mariam.maisuradze3@unibo.it; min.li2@unibo.it; marco.giorgetti@unibo.it; [b] Helmholtz Institute Ulm, Helmholtzstrasse 11, 89081, Ulm, Germany; [c] Karlsruhe Institute of Technology, 76021 Karlsruhe, Germany; angelo.mullaliu@kit.edu; stefano.passerini@kit.edu; [d] ALBA Synchrotron Light Source, Carrer de la Llum 2-26, 08290 Cerdanyola del Vallés, Spain; [e] Institut de Ciència de Materials de Barcelona, Consejo Superior de Investigaciones Científicas, 08193 Cerdanyola del Vallès, Spain; asorrentino@cells.es; dino.t@csic.es; [f]ELETTRA Sincrotrone Trieste S.C.p.A., 34149 Trieste, Basovizza, Italy; ilaria.carlomagno@elettra.eu; giuliana.aquilanti@elettra.eu; jasper.plaisier@elettra.eu.

ABSTRACT

Prussian Blue (PB) and its analogues (PBAs) are large family of transition metal hexacyanoferrates with general formula of $A_xM[Fe(CN)_6]_\gamma\square_{1-\gamma}\cdot zH_2O$. They have open framework structure, redox-active sites and strong structural stability. Among simple PBAs, manganese hexacyanoferrate (MnHCF) displayed a high specific capacity and redox plateaus at high voltage [1] in half cells against both Li and Na. MnHCF was easily to synthesize with co-precipitation method. Its structure and characteristics were investigated with several conventional and synchrotron techniques. After cycling some changes might occur concerning the charge states of the different elements inside MnHCF. For investigation of this phenomenon synchrotron techniques are particularly informative. Energy-dependent full field transmission soft X-ray microscopy (TXM) is able to give a full picture at the nanometer scale of the chemical state and spatial distribution of the elements inside MnHCF. It provides pixel-by-pixel absorption spectrum, making it possible to select groups of pixels and map regions with the similar spectral features [2]. Especially important for this study is observation of inhomogeneous state of charge within the electrode. For the same purpose another imagining technique, the two-dimensional X-ray fluorescence spectroscopy (2D-XRF), was used. By tuning the incident energy of the beam, it was observed that the contribution of different charge species is not the same. These two techniques are complementary, in terms of spatial resolution and of sample representativity.

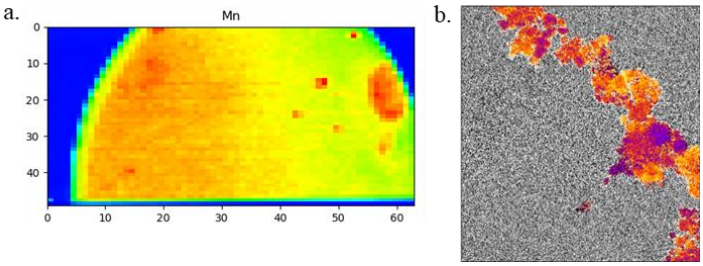

Figure 1. a. 2D-XRF measurement of Mn K edge of the sample LiFC20; b. TXM measurement of Fe L edge of the sample LiC50: ratio map of (Peak A-pre-absorption)/(Peak C-pre-absorption).

Inhomogenities within the samples were identified. With 2D XRF after 20 cycles intercalation was found in the peripheries of charged species analysis, while with TXM analysis randomly distributed intercalated regions were observed after 50 cycles.

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P32 – DEVELOPMENT OF A NEW LIGAND BASED ON AMINO-PYRIMIDINE CURCUMIN FOR THERANOSTIC APPLICATIONS

Matteo Mari,[a] Debora Carrozza,[a] Michele Iori,[b] Pier Cesare Capponi,[b] Sara Rubagotti,[b] Mattia Asti,[b] Erika Ferrari [a]

[a] Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia, via G. Campi 103, 41125, Modena, Italy

[b] Radiopharmaceutical Chemistry Section, Nuclear Medicine Unit, Azienda USL-IRCCS Reggio Emilia, via Amendola 2, 42122, Reggio Emilia, Italy

ABSTRACT

Curcumin is well known for its countless therapeutic properties, including antitumor, anti-inflammatory, and antimetastatic activities, as well as inhibitory of angiogenesis [1]. These features, together with its high affinity for colon-rectal cancer cells, makes it a feasible targeting vector for theranostic purposes [2]. On the other hand, curcumin issues are: low solubility in water, low rate of intestinal absorption and rapid degradation in physiological media. The latter could be attributed to the presence of the β-diketo moiety that make it a challenging compound to deal with. Platinum complexes, cisplatin and oxaliplatin above all, are nowadays widespread and well-known therapeutics for the treatment of several cancers, mainly prostate, ovarian and colorectal [3]. On the other hand, copper isotopes, are used for both diagnosis and therapy in nuclear medicine applications [4].

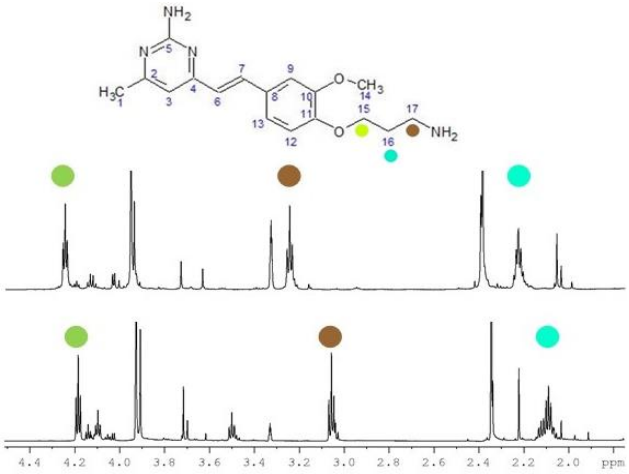

Figure 7. ^{1}H NMR spectra of: MPYC3NH2 in MeOD-d_4 (bottom) and K_2PtCl_4:MPYC3NH2 1:1 after 1 week in MeOD-d_4/D_2O (top) at 298 K @ 600 MHz.

Developing ligands for copper(II) and platinum(II) based on a curcumin structure with improved water solubility and stability may lead to theranostic compounds that benefit of either the metal properties and the antiproliferative activity of curcumin as well. To accomplish this purpose, the new compound MPYC3NH2 (Figure 1) was synthesized. In this new derivative, the β-diketo moiety was replaced with an amino-pyrimidine ring and the phenolic group was functionalized with an amino-alkyl chain. This terminal amine is meant to act both as coordinating agent and as reactive group for further structural modifications. The molecular weight below the cut-off value of 500 Da in combination with the presence of polar groups may account for sufficient water solubility and cellular uptake. A complete ^{1}H/^{13}C NMR characterization with both 1D and 2D techniques was carried out, as well as the acid-base behaviour by spectrophotometric techniques. UV-vis data allowed to evaluated protonation stability constants. UV-vis complexation studies were performed with Cu^{2+} while the complexation with Pt^{2+} was investigated by ^{1}H and ^{195}Pt NMR. As shown in Figure 1, proton spectra point out downfield shifts of signals belonging to the amino-alkyl chain. This outcome indicates the formation with slow kinetics of a metal-complex species. In particular, the ^{1}H-NMR most affected signal is the one belonging to the -CH_2 directly bound to the amine group, while the shift affecting the -CH_2 protons in β and γ positions is less evident.

Concluding, these preliminary results are encouraging and suggest that these studies may lead to a new class of compounds although further biological studies need to be carried out.

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P33 – GREEN SOLID PHASE PEPTIDE SYNTHESIS: ALTERNATIVE SOLVENT AND BASE

Alexia Mattellone,[a] Giulia Martelli,[a] Paolo Cantelmi,[a] Chiara Palladino,[a] Dario Corbisiero,[a] Tommaso Fantoni, Alessandra Tolomelli,[a] Marco Macis,[b] Antonio Ricci,[b] Walter Cabri,[a] Lucia Ferrazzano [a]

[a] P4i Lab, Department of Chemistry, Alma Mater Studiorum University of Bologna, Via Selmi 2, 40126, Bologna, Italy

[b] Innovation and Development¸ Fresenius Kabi iPsum, via San Leonardo 23, 45010 RO, Italy

ABSTRACT

The success of peptides in several therapeutic areas is directly related to the availability of reliable synthetic techniques that allowed medicinal chemists to better explore this molecular space. Nowadays, several technologies can be used for the synthesis of pharmaceutical grade polypeptides, but solid-phase peptide synthesis (SPPS) is still playing a central role in this context. [1]

The main components of SPPS wastes in the upstream process are solvents (80-90% of waste) and the most widely used is *N*,*N*-Dimethylformamide (DMF) which is reprotoxic. Piperidine is the main popular base for Fluorenylmethyloxycarbonyl (Fmoc) removal. Since it is employed to produce drug intermediates, its sale is regulated by strict controls. For these reasons, we explored greener alternatives for solvent and base. First, we identified *N*-octyl pyrrolidone (NOP) as the best candidate. NOP showed good performances in terms of swelling, coupling efficiency and low isomerization generating peptides with very high purity. A mixture of NOP with 20% dimethyl carbonate (DMC) allowed a decrease in solvent viscosity, making the mixture suitable for the automated solid-phase protocol. [2] Then, we have investigated the use of alternative bases with good greenness scores that are able to efficiently deprotect the Fmoc moiety without interfering with the SPPS of the growing peptide. We evaluated deprotection time, racemization ratio, dibenzofulvene trapping and aspartimide formation comparing Diethyltrimethylenediamine (DEAPA) and piperidine in NOP and DMF. DEAPA proved to be an efficient base for Fmoc removal in SPPS upstream processes.

Based on these considerations, Aib-enkephalin and linear octreotide were successfully synthesized to test the designed methodologies achieving the same results than DMF and piperidine. In these experiments, NOP, DMC and DEAPA could be easily recovered by direct distillation from the process waste mixture. The process mass intensity (PMI), being reduced by 63 – 66%, achieved an outstanding value representing a clear step forward in achieving green SPPS. [3]

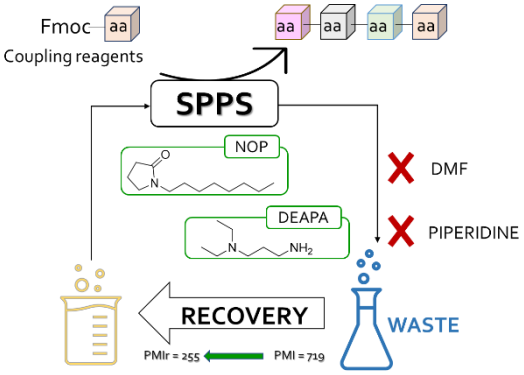

Figure 1: Figurative image of the green SPPS.

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P34 – COBALT-IRON PRUSSIAN BLUE AS OVERLAYERS FOR PHOTOELECTROCHEMIAL $BiVO_4/WO_3$ JUNCTIONS

Michele Mazzanti, Stefano Caramori, Vito Cristino
Dipartimento di Scienze Chimiche e Farmaceutiche ed Agrarie, Università degli Studi di Ferrara, Via Luigi Borsari 46, 44121 Ferrara, Italy
E-mail: mzzmhl3@unife.it

ABSTRACT

The production of hydrogen from the water splitting using solar energy is a key goal of photoelectrochemistry, since solar is one of the most appealing and widely distributed energy sources. In principle, semiconductor-based devices provide the most straightforward route to a cheap and tunable process for the direct conversion of sunlight into solar fuels, as they can store for a short period the photon energy by creating a moving electron-hole pair that can be used for water reduction and oxidation processes.
Metal oxides such as WO_3 and $BiVO_4$ are good candidate photoanodes for water oxidation. $BiVO_4$, a semiconductor that can be prepared in a nano-structured form with interesting spectral absorption characteristics (E_{gap} ca. 2.5 eV) and values of the valence and conduction bands that make it suitable for applications in photo electrolysis for the production of solar hydrogen [1]. Unfortunately, the low mobility of the charge carriers and the less than ideal stability under polarization and illumination conditions preclude its effective use as a single junction. The formation of n-n junctions on porous materials such as WO_3 is a promising approach to solve the problem of poor mobility of $BiVO_4$ carriers.

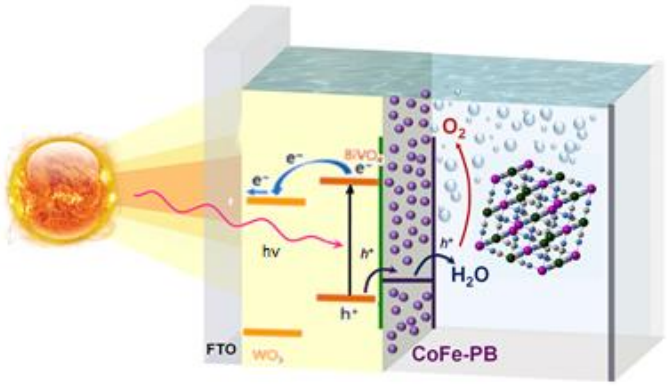

Figure 1. Schematic representation of water oxidation process using $WO_3/BiVO_4$/CoFe-BP

Efficient charge separation in the n-n junction still requires additional positive potential to counter carrier recombination. A common approach to reduce the need for such strong positive potential is the exploitation of an electrocatalyst on the surface of the photoanode to act as a hole transfer medium, contributing to decouple electrons and holes. Cobalt hexacyanoferrate, the cobalt−iron analogue of Prussian blue (CoFe-PB), is a robust, effective, and inexpensive water oxidation electrocatalyst. CoFe-PB modification of $WO_3/BiVO_4$ photoanodes produces substantial improvements in both the onset potential and stability in neutral conditions. [2]

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P35 – HETEROGENEOUS PHOTOCATALYSIS FOR THE REDUCTIVE TRANSFORMATION OF HALOGENATED POLLUTANTS

Martina Milani, Alessandra Molinari, Tatiana Chenet, Luisa Pasti
Dipartimento di Scienze Chimiche, Farmaceutiche ed Agrarie, Università di Ferrara, via Luigi Borsari 46, 44121 Ferrara, Italia.
E-mail: martina.milani@unife.it, alessandra.molinari@unife.it, tatiana.chenet@unife.it, luisa.pasti@unife.it

ABSTRACT

Photocatalysis is an environmentally friendly technique aimed to the removal of different types of pollutants. It is based on the formation *in situ* of $^{\bullet}OH$ radicals, that contribute to the oxidative degradation of molecules. For this reason, photocatalysis belongs to the advanced oxidation processes (AOPs). Titanium dioxide (TiO_2)[1] is the most studied material but also other semiconducting oxides and their model systems such as polyoxometalates[2] are employed as photocatalysts. The goal of oxidative degradation is mineralization, that is the complete degradation of the pollutant to CO_2 and water. However, this process is not easy to achieve, and often only partial oxidation produces intermediates that are more toxic than the starting pollutant.
Much less attention has been paid to the exploitation of photocatalysts in reductive processes that use electrons promoted in the conduction band (CB) of photoexcited semiconductors. Recent literature shows that it is possible to carry out hydrogenation[3] and deoxygenation reactions[4], so producing new interesting molecules from pollutants.
The thesis and the PhD project focus on reductive transformation of halogenated pollutants by using heterogeneous photocatalysts in proper reaction conditions under solar light irradiation. For example, cadmium sulfide (CdS) and decatungstate based photocatalysts have been studied for the transformation of pentachlorophenol (PCP) and dieldrin. These pollutants are significantly transformed during irradiation as shown in Figure 1: CdS transforms the 75% of PCP in 60 minutes when irradiated with visible light and decatungstate immobilized on an anionic exchange resin (Amb/DTA) converts 50% of dieldrin in 120 minutes when irradiated with near UV light. The heterogeneous character of the employed photocatalysts makes them easily recoverable and recyclable.

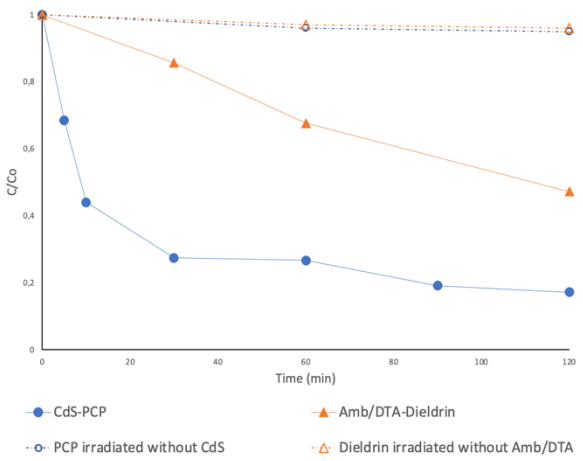

Figure 1. C/C_0 of pollutant vs. irradiation time (min). Full symbols: in the presence of photocatalyst. Empty symbols: in the absence of photocatalyst. Reported data are the mean of 3 repeated experiments. Errors are ± 5%.

As for reaction mechanism, ESR spin trapping investigation gave evidence that it is the electrons that are accepted by the halogenated molecules, likely initiating dehalogenation reactions. This result would open the way to a new halogenated pollutants treatment for their removal from the environment since it could allow the formation of intermediates with less chlorine atoms and, because of this, less dangerous.

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P36 – NOVEL ELECTRO-ANALYTICAL APPROACH FOR THE DETECTION AND DISCRIMINATION OF CANNABINOIDS IN REAL SAMPLES EXTRACTS

Alessandro Monari,[a] Gabriele Bevini,[a] Barbara Zanfrognini,[b] Chiara Zanardi,[a,b] Laura Pigani,[a] Giorgia Foca,[c] Alessandro Ulrici [c]

[a] Department of Chemical and Geological Sciences, University of Modena and Reggio Emilia, via Campi 103, 41125 Modena, Italy

[b] Institute of Organic Synthesis and Photoreactivity (ISOF), National Research Council of Italy (CNR), Via P. Gobetti 101, 40129 Bologna, Italy

[c] Department of Life Sciences, University of Modena and Reggio Emilia, via Amendola 2, 42122 Reggio Emilia, Italy

ABSTRACT

Cannabinoids are terpenophenolic compounds of great interest which have been extensively investigated due to their important pharmacological properties. Phytocannabinoids are cannabinoids derived from Cannabis sativa L; among them, trans-Δ^9-tetraidrocannabinol (THC) is widely known for its psychoactivity while cannabidiol (CBD), which is non-psychoactive, is known for its neuroprotective, anti-inflammatory and analgesic characteristics. Marijuana and hashish, referred as recreational Cannabis, are illicit products possessing high THC levels and low CBD levels, while some fiber-type Cannabis products (including those known as "Cannabis light") have been recently legalized in many countries. This type of products present on the market are growing exponentially, urging the need of an accurate controls to meet specific regulations. The determination of cannabinoids in real samples and the determination of THC/CBD ratio is performed with the use of chromatographic techniques; however, the non-portable instrumentation, the consuming sample preparation and the long analysis time don't allow for their use in in-situ analysis. As promising alternatives to these techniques in allowing a real-time and fast cannabinoid screening, electrochemical sensors have been receiving considerable interest, thanks to their low cost, handiness and miniaturization possibility [1]. In fact, THC, CBD and their natural acidic precursors (i.e. THCA and CBDA) are electroactive, due to the oxidation of the phenolic group, that makes them good candidates for electrochemical analysis. This work was then focused on the development of sensors exploiting the electroactivity of cannabinoids to perform qualitative and quantitative analysis even in real matrices extracts. Among all the electrodic materials tested, screen printed electrodes (SPEs) modified with carbon black (CB) showed very promising results [2]. The sensor ability to recognize various Cannabis samples has been investigated coupling voltammetric techniques to chemometric data analysis. Initial experiments have been developed in aqueous/methanol mixtures containing THC or CBD and both; then measurements have been performed on real samples represented by extracts of different types of cannabis. The electrochemical procedure proposed, together with the good detection performances of SPE-CB electrodes, lead to excellent results, allowing the discrimination between samples with different CBD and THC content.

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P37 – CARBON NANOSTRUCTURES DECORATED WITH CERIUM OXIDE AS MULTI-FUNCTIONAL ELECTROCATALYSTS FOR CO_2 REDUCTION

Miriam Moro,[a] Giovanni Valenti,[a] Tiziano Montini,[b] Lucia Nasi,[c] Michele Melchionna,[b] Giovanni Bertoni,[c] Marcella Bonchio,[d] Paolo Fornasiero,[b] Francesco Paolucci,[a] Maurizio Prato [b]

[a] Department of Chemistry "Giacomo Ciamician", Alma Mater Studiorum - University of Bologna, Via Selmi, 2 - 40126 Bologna, Italy

[b] University of Trieste, Dep. of Chemical Science, Center of Excellence of Nanostructured Material (CENMAT), Trieste, Italy

[c] CNR-IMEM Institute, Parco area delle Scienze 37/A, 43124 Parma, Italy

[d] University of Padova, Via F. Marzolo 1, 35131 Padova, Italy

E-mail: miriam.moro2@unibo.it

ABSTRACT

The electrocatalytic reduction of CO_2 is a captivating strategy for the conversion of CO_2 into fuels, to realize a close loop for carbon footprinting. The research has focused on the development of new materials and technology capable of capturing and converting CO_2 into useful products.[1] Among all reduction products, formic acid is particularly attractive for its high volumetric hydrogen density, low toxicity, and liquid state, that make it a valuable hydrogen storage vector.

The design of new electrocatalysts that reduce CO_2 in a selective and efficient fashion is a key step for future exploitation of this technology.

Here we present how the combination of different building blocks in a single nanostructure might be a good strategy to achieve a good selectivity in the CO_2 reduction process.

Combining the unique physico-chemical properties of functionalized nanomaterials (such as carbon nanotubes and carbon nanohorns) and nanocrystalline cerium dioxide (CeO_2) we revealed faradaic efficiency for formic acid production as high as 55% at an overpotential as low as 0.02V in acid solutions. These performances have been possible by the formation of partially reduced ceria ($Ce^{4+/3+}O_{2-x}$) responsible of an increased CO_2 adsorption and a more efficient electron transfer at the surface.[2] In the nanocomposite, the carbon nanostructures are used as support and they have a fundamental role in to counteracting the insulating effect of oxide nanoparticles and promoting the generation of Ce^{3+} sites. Their elevated surface area and high electrical conductivity guarantee a greater process efficiency.[3] In particular, the nanohorns have a unique conical geometric, where the nano-tips terminals act as "electron collector", increasing the charge mobility.[4]

We demonstrated that the interconnections between various components are fundamental for the efficient CO_2 reduction to formic acid and opens new possibilities in the design of optimized electrocatalytic materials.

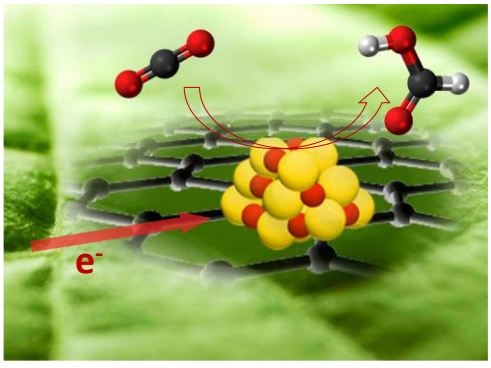

Figure 8. Schematic CO_2 reduction into formic acid on MWCNT@CeO_2

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P38 – LIGHT-HARVESTING ANTENNAE BASED ON COPPER INDIUM SULFIDE (CIS) QUANTUM DOTS

Giacomo Morselli,[a] Alessandro Gradone,[a,b] Vittorio Morandi,[b] Paola Ceroni [a]
[a]Department of Chemistry "Ciamician", University of Bologna, Via Selmi 2, 40126, Bologna, Italy.
[b]CNR-IMM Bologna Section, Via Piero Gobetti 101, 40129 Bologna, Italy
E-mail: giacomo.morselli2@unibo.it, paola.ceroni@unibo.it

ABSTRACT

Quantum dots (QDs) are considered to be ideal luminophores, due to their size-dependent properties, including absorption and emission spectra and electrochemical properties. Copper indium sulfide quantum dots (CIS QDs), in particular, are valid alternatives to conventional lead and cadmium-containing quantum dots due to their non-toxicity and good optical properties. In fact, CIS QDs exhibit high molar absorption coefficients over the entire visible spectral region (10^4-10^5 $M^{-1}cm^{-1}$), elevated photoluminescence quantum yields (up to 70%) and long emission lifetimes (hundreds of nanoseconds).[1,2]
The quantum dot properties can be ameliorated by functionalizing its surface with molecules that can provide new features. For instance, fluorophores can be conveniently used for the functionalization of the QDs to improve the optical properties of the nanoparticle. Our group previously reported the decoration of silicon nanoparticles with a large number of chromophores that efficiently absorb the incoming light and then channel it to the quantum dot, which can emit with a higher brightness.[3,4] Such systems are called *light-harvesting antennae* and are useful for all the applications that require elevated absorption and emission intensities, such as luminescent solar concentrators and bioimaging. Here, we describe the functionalization of CIS QDs with a ligand containing a UV-absorbing chromophore, namely pyrene, by a ligand exchange strategy. The pyrene-functionalized nanoparticles are characterized by a superior absorption below 350 nm and a sensitized emission of the CIS QD upon pyrene excitation due to energy transfer from the organic chromophore towards the quantum dot. This represents the first example of a light-harvesting antenna based on copper indium sulfide quantum dots with enhanced brightness compared to the pristine sample without pyrene chromophores at the surface.

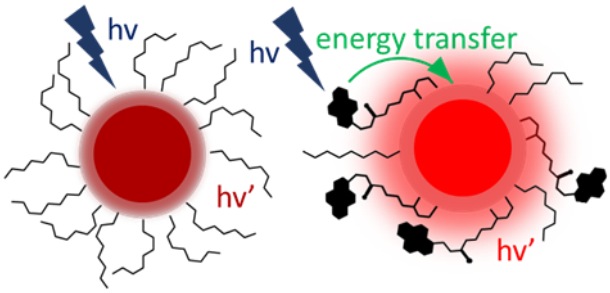

Figure 1. Comparison between the photoluminescence of alkyl-passivated (on the left) and fluorophore-functionalized (on the right) quantum dot.

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P39 – PCR-FREE VIRAL GENOME DETERMINATION BY ELECTROGENERATED CHEMILUMINESCENCE

Pavlos Nikolaou,[a] Salvatore Petralia,[b] Alessandra Zanut,[a,c] Giovanni Valenti,[a] Sabrina Conoci,[d] Luca Prodi,[a] Francesco Paolucci [a]

[a] Department of Chemistry "Giacomo Ciamician", University of Bologna, Via Selmi 2 40216, Bologna, Italy

[b] Dipartimento di Scienze del Farmaco e della Salute, University of Catania, Viale Andrea Doria, 6 - 95125 Catania, Italy

[c] Department of Chemical and Biomolecular Engineering, New York University, 6 Metrotech, Brooklyn, NY, 11201 USA

[d] Dipartimento di Scienze Chimiche, Biologiche, Farmaceutiche ed Ambientali, University of Messina, Viale Ferdinando Stagno d'Alcontres, 31 - 98168 Messina, Italy

ABSTRACT

Electrochemiluminescence or Electrogenerated Chemiluminescence (ECL) is an electrochemical technique with a simple instrumentation which is based on a luminescent phenomenon, produced from an electron-transfer reaction taking place on the surface of the electrode and yielding light-emitting excited states. The most know luminophores/coreactant system in aqueous media is tris(2,2'-bipyridine) ruthenium(II) ($[Ru(bpy)_3]^{2+}$)/tri-n-propylamine with important analytical application in commercial assays for the detection of biomarkers. [1,2] According to World Health Organization (WHO) Hepatitis B Virus (HBV) is the main problem of the infection of 257 million people. [3] An ECL-based and also PCR-free sensor is developed for the determination of the double-standed DNA of HBV (ds-DNA). The ds-DNA of HBV has been immobilized and remained anchored between two monoclonal oligonucleotide chains probes (P1 and P2), thus the same time the triplex formation is created via Hoogstern H-bonds (Figure 1a). [4] The ECL-active molecule $[Ru(phen)_2dppz]^{2+}$ it can be remained intercalated in the ds-DNA according to the π-π* stalking intercalation -dppz. [5] The ECL-based sensor is tested in a range from 0-10000 copies μL^{-1} obtaining a limit of detection of 2.4 copies μL^{-1} which is much more sensitive, comparing it with

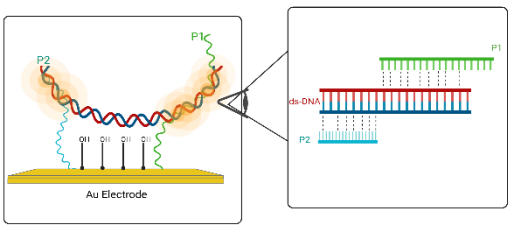

Figure 1: Immobilization of specific probes and triplex formation between ds-DNA of HBV and P1, P2 probes.

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P40 – NBR/PEO NANOFIBROUS MEMBRANE FOR ENHANCING INTERLAMINAR FRACTURE TOUGHNESS IN CFRP LAMINATES

Jacopo Ortolani,[a] Emanuele Maccaferri,[a] Laura Mazzocchetti,[a,b] Tiziana Benelli,[a,b] Tommaso Maria Brugo,[b,c] Andrea Zucchelli,[b,c] Loris Giorgini [a,b]

[a] Department of Industrial Chemistry "Toso Montanari", University of Bologna, Viale Risorgimento 4, 40136 Bologna, Italy; E-mail: jacopo.ortolani3@unibo.it, emanuele.maccaferri3@unibo.it, laura.mazzocchetti@unibo.it, tiziana.benelli@unibo.it, loris.giorgini@unibo.it

[b] Interdepartmental Center for Industrial Research on Advanced Applications in Mechanical Engineering and Materials Technology, CIRI-MAM, University of Bologna, Viale Risorgimento 2, 40136 Bologna, Italy; E-mail: tommasomaria.brugo@unibo.it, a.zucchelli@unibo.it

[c] Department of Industrial Engineering, University of Bologna, Viale Risorgimento 2, 40136 Bologna, Italy

ABSTRACT

Two main drawbacks significantly affect Carbon Fiber Reinforced Polymer (CFRP) laminates: delamination and low damping. Based on recent studies regarding the electrospinning of polymeric blends [1,2], this work presents the production, via electrospinning, of rubbery nanofibers made of Nitrile Butadiene Rubber / Polyethylene oxide (NBR/PEO) for hindering delamination in CFRP laminates. The resulting nanofibrous morphology (**Figure 1**) is stable-over-time without any additional crosslinking step after electrospinning. The mat shows sufficient mechanical properties to allow its integration into the CFRP laminates. Tensile tests were carried out to mechanically characterize the membrane. Load data were normalized by taking into account the specimen mass instead of its cross-section area, by applying the following equation [2]:

$$\sigma = \rho \frac{F}{m} L$$

where σ is the stress, m is the specimen mass, ρ is the polymer blend density, L is the specimen initial length, and F is the force. Moreover, tensile data were analyzed with a phenomenological fitting model [3]. The performance of the NBR/PEO nano-modified composite will be investigated via Double Cantilever Beam (DCB) test, and compared with unmodified CFRP. The integration of such nanofibrous mats in any area of the laminate allows to contrast delamination problems related to high stress concentration in particular regions, such as geometric discontinuities, making this approach versatile and flexible. The achieved results are very encouraging and pave the way to the use of NBR/PEO nanofibrous mats for hindering delamination in composite laminates.

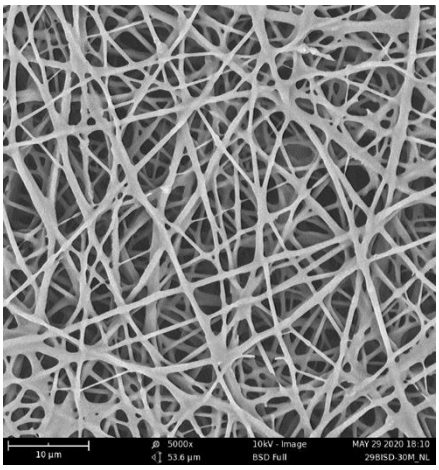

Figure 1. *NBR/PEO nanofibrous mat. Scale bar: 10 µm, 5000x.*

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P41 – IBUPROFEN AND IBUPROFEN-PARACETAMOL CONJUGATE POLYMERIC NANOPARTICLES FOR TRAUMATIC BRAIN INJURY

Ilaria Ottonelli,[a] Vito Antonio Baldassarro,[b] Riccardo Caraffi,[a] Maria Vittoria Grazioli,[a] Giovanni Tosi,[a] Maria Angela Vandelli,[a] Barbara Ruozi,[a] Laura Calzà [b]

[a] Nanotech Lab, Te.Far.T.I., Dept. Life Sciences, University of Modena and Reggio Emilia, Italy, 41125; E-mail: ilaria.ttonelli@unimore.it

[b] Interdepartmental Center for Industrial Research - Life Sciences and Technology, University of Bologna, Italy, 40064

ABSTRACT

Traumatic brain injury (TBI) is the most common cause of death and disability in the last few decades. It is a combination of anatomical and functional damage caused by external forces. This first insult triggers a cellular cascade consisting of molecular, chemical, and inflammatory response which can be responsible for comatose state until death. In particular, inflammatory effects led to the activation of cytokine cascade that cause a neuronal degenerations. Many pharmacological therapies have been tested for TBI treatment such as corticosteroids and anti-inflammatory drugs, but the high doses required and need for repeated administrations is still a problem. For this reason, the formation and optimization of nanosystems may be the key to obtain a prolonged release and reduce the number of administrations while allowing for the potential targeting to the brain.

In this context, FDA approved polymers such as PLGA and PLA to formulate nanoparticles (NPs) have been used for their biocompatibility, biodegradability, and their suitability for encapsulation and sustained/prolonged release of pharmaceutic molecules. In particular, Ibuprofen and ibuprofen-paracetamol conjugate NPs were formulated to reach anti-inflammatory activity and inhibit neurodegeneration properties.

In this work, formulations containing each individual drug were optimized for encapsulation efficiency and to promote improved release profile kinetics in biologically relevant buffers.

Initially, PLGA and PLA NPs loaded with ibuprofen were prepared changed several parameters like organic and aqueous phase ratio, type and percent of surfactants. NPs based on PLA is turned out to be the best formulations in terms of chemical-physical and technological-pharmaceutical properties since the polymer, being more lipophilic than PLGA, it interacts better with ibuprofen.

Unfortunately, ibuprofen NPs gave unpromising results in terms of release because ibuprofen is a small molecule with a poor solubility in water and these properties are responsible for its rapid and un-wanted release. To optimize the formulations, we focus on a conjugation of ibuprofen with paracetamol, another drug able to reduce inflammatory environment at the site of action, to increase the molecular weight to extend the release and evaluate a possible increase of ant-inflammatory activity.

Afterwards, ibuprofen-paracetamol conjugate was encapsulated into polymeric NPs. Chemico-physical and pharmaceutical properties of the different formulations produced highlighted that the increased molecular weight of the molecule improved the encapsulation efficacy (around 50%) with respect to Ibuprofen alone (lower than 30%). Moreover, loading content was improved as well, 2-4mg of Ibuprofen/100 mg of NPs compared to 5-6 mg of ibuprofen-paracetamol conjugate/100 mg of NPs. In vitro, followed by in vivo tests, will be used to confirm possible efficacious and long-term therapeutic effects, leading to a novel option for spinal cord injuries treatment and management.

ACKNOWLEDGEMENTS

This research was partially funded by IMI EU Grants Investigating Mechanisms and Models predictive of accessibility of therapeutics (IM2PACT) Into the Brain IMI2 - Call 12, GA n.807015(im2pact.org), and Ministero degli Esteri e della Cooperazione Internazionale MAECI grant, grant Progetti di ricerca scientifica e tecnologica di grande rilevanza, Ministero degli Esteri, Mat2Rep" ER Project, Bando per progetti di ricerca industriale strategica rivolti agli ambiti prioritari della strategia di specializzazione intelligente" (DGR 986/2018) POR-FESR EMILIA ROMAGNA 2014-2020, Asse 1 – Ricerca e innovazione, Azione 1.2.2.

P42 – A COMPARATIVE STUDY OF TWEEN AND BSA ON ENZYME STABILIZING EFFECTS IN PLGA NMED FORMULATIONS

Ilaria Ottonelli,[a,b] Jason Thomas Duskey,[a] Riccardo Caraffi,[a] Irene Parmeggiani,[a] Arianna Rinaldi,[a,b] Barbara Zambelli,[c] Maria Angela Vandelli,[a] Giovanni Tosi,[a] Barbara Ruozi [a]

[a] Nanotech Lab, Te.Far.T.I., Department. Life Sciences, University of Modena and Reggio Emilia, 41125, Modena, Italy

E-mail: ilaria.ottonelli@unimore.it, jasonthomas.duskey@unimore.it, arianna.rinaldi@unimore.it, mariaangela.vandelli@unimore.it, gtosi@unimore.it, barbara.ruozi@unimore.it

[b] Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, 41125, Modena, Italy

[c] Laboratory of Bioinorganic Chemistry, Department of Pharmacy and Biotechnology, University of Bologna, 40127, Bologna, Italy; E-mail: barbara.zambelli@unibo.it

ABSTRACT

Enzymes are prime candidates for the treatment of central nervous system diseases with the possibility to offer safer, natural and longer-term treatments compared to their small molecule counterparts. Unfortunately, poor results due to loss of activity and poor targeting/biodistribution have been huge limiting factors for Enzyme replacement therapy (ERT). Nanomedicine were the most attractive strategies because enzymes can be loaded into a nanoparticles which can be targeted to brain disease.

Many stabilizing molecules have been investigated to retain the enzyme activity. Unfortunately, most studies focus only on the biological effect of the enzyme, but lack information on the complex between the stabilizer and enzyme during the formulation. This information is critical to understand and compare the stabilizing mechanism of different molecules.

In this work, we compare the effects of two different molecules (Tween® and BSA) for the stabilizer effects on the enzyme β-glucosidase in solutions and during nanoparticle formulation.

In a preliminary study, Tween®20 was discovered to have most stabilizing effects out of the Tween series (Tween® 20, 60, 80). Therefore, varying the molar rapport between the stabilizer and enzyme led to a discernably different effect where Enzyme:BSA formed characterizable complexes while Tween20 did not (studied by ITC, PCS and STEM\AFM microscopy).

During the NP formulation addition ether stabilizer had no effects on the physical-chemical properties of the NP (size, PdI, Zeta-Potential). However, BSA lead to significantly higher encapsulation efficacy of the enzyme compared to Tween (23% and 10%, respectively).

Increasing the stabilizer molar rapport of ether stabilizer led to a directly proportional increase in a enzyme activity compared to non-stabilizer formulations.

In release studies, both stabilizers led to longer release profiles with higher enzyme activity in the release buffer. Finally, combing the stabilizers into a single NP formulation led to additive effect with proportional high activity. This result highlights the important of more well define characterization studies of different enzyme stabilization systems.

ACKNOWLEDGEMENTS

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P43 – BIOBASED AND BIODEGRADABLE ELECTROSPUN MEMBRANES ENRICHED WITH CARBON QUANTUM DOTS FOR OIL-SPILL CLEANUP

L. Pesenti,[a] S. Ben Zichri,[b] C. Gualandi,[a] M. L. Focarete,[a] R. Jelinek,[b] P. Galletti [a]
[a] Department of Chemistry "G. Ciamician", University of Bologna, Bologna, Italy
[b] Department of Chemistry, Ben Gurion University of the Negev, Beer Sheva, Israel
E-mail: lucia.pesenti2@unibo.it

ABSTRACT

Nowadays, membrane technology is making an enormous contribution to tackling the worldwide challenge of treating contaminated waters. Among the many different technologies for membrane production, electrospinning is considered extremely valuable to obtain highly porous non-woven fibrous membranes, easily functionalizable with specific compounds to improve their efficiency for tailor-made applications. Carbon quantum dots are a unique class of carbon-based nanomaterials that can be synthesized from carbonaceous building blocks and even from biomass, exhibiting unique biocompatibility. Given their capacity of absorbing light and their photothermal conversion ability, C-dots have recently found application in energy and photocatalytic processes, among which photocatalytic degradation of pollutants, solar-enabled water remediation and oil-spill cleanup.[1,2]
The aim of this work is to develop C-dots-enriched hydrophobic polymeric membranes by electrospinning and to test their use in oil-spill cleanup (Fig.1a). Poly-L-lactic acid (PLLA) was chosen as a biobased and biodegradable hydrophobic polymer and hydrophobic C-dots synthetized from Citric acid: Octadecylamine: Urea (1:1:0.5 gr) were used. Fibers with diameters in the range 600-800 nm and loaded with different amounts of hydrophobic C-dots were prepared and characterized by SEM analysis (Fig. 1b). Thermal properties were studied by means of TGA and DSC analysis, mechanical properties of membranes were assessed by stress-strain tests and wettability was determined by water contact angle measurements. To test membrane efficiency, a solar-simulator-induced-heating experiment was conducted: the membrane sample was heated under a solar simulator for 30 minutes while being immersed in a mixture of castor and silicon oil, mimicking an oil-spill real life scenario. The oil-absorbance capacity (OAC: g oil/g sample) was assessed by weighting the membrane sample before and after immersion in oil. Results show OAC in the range 10-30 g/g and membranes loaded with higher amounts of C-dots display higher heating capacity and higher oil-absorbance capacity. Results are promising and further in-depth research is needed. Moreover, the possibility of selecting C-dots from a biomass source can further improve the sustainability of the production process and the biodegradability of the final product.

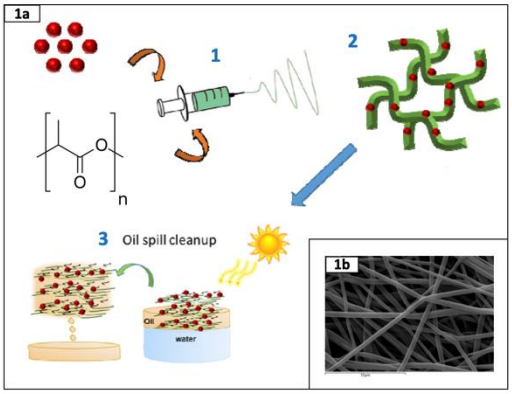

Fig 1a. Membrane production procedure for oil-spill cleanup
Fig 1b. SEM image of PLLA nanofibrous membrane doped with C-dots (scale 10µm)

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P44 – PHOTOCATALYTIC CROSS-DEHYDROGENATIVE COUPLING OF ARYL-GLYCINE MEDIATED BY MESOPOROUS GRAPHITIC CARBON NITRIDE IN GREEN SOLVENT: A ROUTE TO INDOLE-DECORATED NON PROTEINOGENIC AMINO-ACID

Lorenzo Poletti,[a] Graziano Di Carmine,[a] Daniele Ragno,[a] Alessandra Molinari,[a] Alessandro Massi,[a] Olga Bortolini [b]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences (DOCPAS), University of Ferrara, Via L. Borsari 46, 44121-Ferrara, Italy

[b] Department of Environmental and Prevention Sciences, University of Ferrara, Via L. Borsari 46, 44121-Ferrara, Italy

E-mail: lorenzo.poletti@unife.it

ABSTRACT

In recent years, the mass production of consumer goods has led to an improvement in living conditions, but this caused an excessive growth of waste and contaminants. In order to limit the production of toxic by-products to humans and environment, modern chemistry has revised its position within society, accentuating efforts to develop new methodologies in a more sustainable perspective. The main challenge is to apply in the best way the principles of "green chemistry" while maintaining high production of key compounds in pharmaceutical, energy and materials sectors [1]. In this spirit, this work leads to the development of a methodology for the synthesis of key intermediates in the pharmaceutical sector [2], which are non-proteinogenic amino acids with indolic scaffold, under eco-sustainable conditions (Figure 1). The use of light as activation energy, which is a clean and renewable energy source, combined with the use of a heterogeneous, metal-free and recyclable photocatalyst such as mesoporous carbon nitride (mpg-CN) brings several benefits to the synthesis of these compounds.

The photocatalyst plays the role of promoter of the reaction through light absorption which modifies its electronic properties. In its excited state, the catalyst activates atmospheric oxygen by favoring a selective oxidation reaction of the aryl glycine which is converted *in-situ* into an electrophilic imine, prone to react with an indolic nucleophile. Moreover, since the catalyst is heterogeneous, recovery and reuse are possible at the end of the process.

Through the reaction of photocatalyzed oxidative coupling, this work has allowed to synthesize a library of non-proteinogenic amino acids "decorated" with indole and aryl glycine of different types that allowed to understand how the reaction behaves by changing the type of substituents on the protagonists of the reaction.

This work has therefore made it possible to improve the synthesis of these compounds following a more eco-sustainable way and making the entire synthetic process easier.

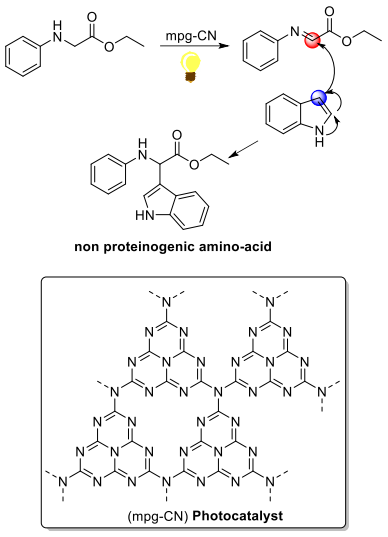

Figure 1. General scheme of the photocatalyzed reaction.

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P45 – COCRYSTALLIZATION PROCEEDING THROUGH A METASTABLE LIQUID: A THOROUGH STUDY VIA MULTI-TECHNIQUES APPROACH

Michele Prencipe,[a] Paolo P. Mazzeo,[a,b] Matteo Masino,[a] Torvid Feiler,[c] Franziska Emmerling,[c] Alessia Bacchi [a,b]

[a] Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università degli Studi di Parma, Parma, Italy, https://scvsa.unipr.it

[b] Biopharmanet-TEC, Università degli Studi di Parma, via Parco Area delle Scienze 27/A, 43124 Parma, Italy, https://www.centritecnopolo.unipr.it/biopharmanet-tec

[c] BAM Federal Institute for Materials Research and Testing Richard-Willstatter-Str. 11, 12489 Berlin, Germany, https://www.bam.de

ABSTRACT

Cocrystallization is the art of combing different molecules (i.e., coformers) to make them interact in a new crystal structure. So far, the comprehension of the cocrystallization process has still appeared as a hard task since may involve several species and requires a full understanding of the molecular dynamics. Many examples of cocrystallization have evidenced the presence of amorphous intermediates [1,2], either solid or liquid, however liquid one have attracted more attention because they enhancing in molecular diffusion which is supposed to encourage cocrystal formation. This aspect has been widely studied for mechanochemical synthesis, that exploit the local energy produced from mechanical stress to induce chemical transformations [3]. However, the use of a kind of investigation may not be enough to a full understanding of an entire process.

For this purpose, we propose a multi-techniques approach which takes advantage of several investigations to examine a cocrystallization process from different points of view. In particular, we focused on the cocrystallization reaction between thymol (THY) and 4,4'-azopyridine (AZO), both solid at ambient conditions, which occur through a metastable liquid phase, giving the AZO-THY 1:2 cocrystal. We coupled an in-situ approach (TRIS-XRPD, Raman spectroscopy) with a calorimetric study (DSC, VT-XRPD) to investigate the AZO-THY conversion mechanism and determine the metastable liquid composition. The metastable liquid resulted to act as medium increasing the molecular mobility and diffusion of the coformers. TRIS-XRPD data analysis on mechanochemical reaction pointed out that the conversion process advanced with a two-step mechanism where, at first, the liquid intermediate was formed and then it rapidly converted into AZO-THY 1:2 cocrystal. Moreover, a new cocrystal (AZO-THY 2:1) has been discovered which presents an incongruent melting point and whose formation involved another liquid phase.

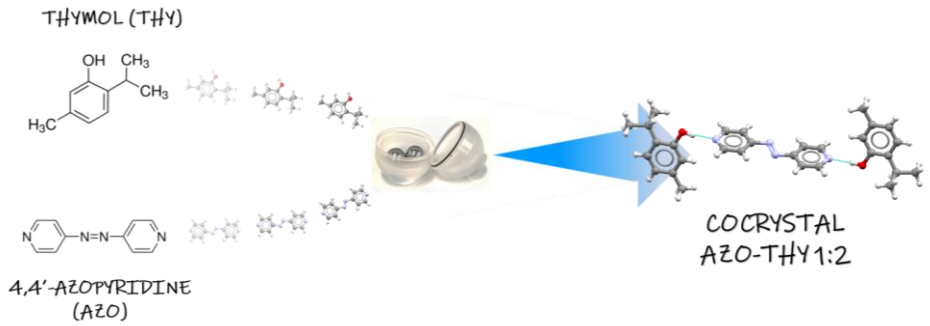

Figure 1. Scheme of mechanochemical cocrystallization between thymol and 4,4'-azopyridine.

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P46 – CHEMOENZYMATIC STEREODIVERGENT SYNTHESIS OF ALL THE STEREOISOMERS OF THE 2,3-DIMETHYLGLYCERIC ACID ETHYL ESTER

Francesco Presini,[a] Graziano di Carmine,[a] Pier Paolo Giovannini,[a] Virginia Cristofori,[a] Lindomar Alberto Lerin,[a] Olga Bortolini,[b] Claudio Trapella,[a] Anna Fantinati [b]

[a] Department of Chemistry, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via Luigi Borsari, 46, 44121 Ferrara, Italy

[b] Department of Enviromental and Prevention Sciences, University of Ferrara, Via Luigi Borsari, 46, 44121 Ferrara, Italy

E-mail: francesco.presini@edu.unife.it, gvnppl@unife.it

ABSTRACT

The 2,3-dihydroxy-2-methylbutyric acid, also known as 2,3-dimethylglyceric acid, constitutes the acyl and/or the alcoholic moiety of many bioactive natural esters. Herein, we describe a chemoenzymatic methodology which gives access to all the four possible stereoisomers of the 2,3-dimethylglyceric acid ethyl ester. The racemic ethyl α-acetolactate, produced by N-heterocycle carbene (NHC)-catalyzed coupling of ethyl pyruvate and methylacetoin has been employed as the starting material. The racemic mixture has been resolved through (S)-selective reductions, pro-moted by the acetylacetoin reductase (AAR) affording the resulting ethyl (2R,3S)-2,3-dimethylglycerate; the isolated remaining (S)-ethyl α-acetolactate has been successively treated with baker's yeast to obtain the corresponding (2S,3S) stereoisomer. syn-2,3-Dimethylgliceric acid ethyl ester afforded by reducing the rac-α-acetolactate with $NaBH_4$ in the presence of $ZnCl_2$ was kinetically resolved through selective acetylation with lipase B from Candida antarctica (CAL-B) and vinyl acetate to access to (2S,3R) stereoisomer. Finally, the (2R,3R) stereoisomer, has been prepared by C3 epimerization of the (2R,3S) stereoisomer recovered from the above kinetic resolution, achieved through the TEMPO-mediated oxidation, followed by the reduction of the produced ketone with $NaBH_4$. The resulting 2,3-dimethylglicertate enriched in the (2R,3R) stereoisomer was submitted to stereospecific acetylation with vinyl acetate and CAL-B in order to separate the major stereoisomer.

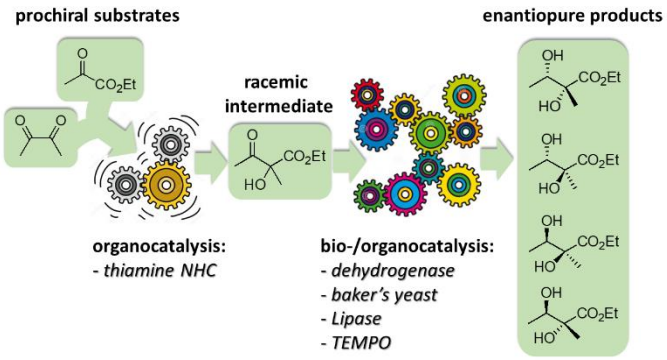

Figure 1. Schematic representation of the whole chemoenzymatic synthesis.

The entire procedure, allowed to convert the racemic α-acetolactate into the four enantiopure stereoisomers of the ethyl 2,3-dihydroxy-2-methylbutyrate with the following overall yields: 42% for the (2R,3S), 40% for the (2S,3S), 42% for the (2S,3R) and 20% for the (2R,3R).

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P47 – SYNTHESIS AND BIOLOGICAL INVESTIGATION OF PACLITAXEL-BILE ACID HYBRIDS

Lorenzo Preti,[a] Elena Marchesi,[b] Elisabetta Melloni,[c] Arianna Romani,[c] Erika Raimondi,[c] Fabio Casciano,[c] Paolo Marchetti,[a] Maria Luisa Navacchia,[d] Daniela Perrone [b]

[a] Dipartimento di Scienze Chimiche, Farmaceutiche ed Agrarie, Università degli studi di Ferrara, Via Luigi Borsari, n. 46 – 44121 Ferrara

[b] Dipartimento di Scienze dell'Ambiente e della Prevenzione Corso Ercole I d'Este 32 44121 – Ferrara

[c] Dipartimento di Medicina Traslazionale e per la Romagna, Via Fossato di Mortara 70 44121 – Ferrara

[d] Istituto per la Sintesi Organica e la Fotoreattività, Via P. Gobetti 101 – 40129 Bologna

ABSTRACT

Paclitaxel is a powerful antitumoral currently used against a broad spectrum of cancers. Its antitumoral action is due to its microtubule stabilization capacity, which impedes proper mitosis and arrests the cell cycle, ultimately causing apoptosis[1]. However, the high potencey of paclitaxel is also a problem as it causes side effects such as neutropenia and apoptosis of normal cells[1]. Paclitaxel has been modified by many research groups to improve its pharmacological profile and its delivery[2,3]. It has been ascertained that the 2'-hydroxyl is vital for tubulin binding and thus to the drug activity, while the 7-hydroxyl can be used to obtain conjugates or link fluorophore units[4]. We reasoned that by conjugating bile acid such as ursodeoxycholic and chenodeoxycholic acid on the 2'-hydroxyl of paclitaxel by esterification a more bio-available prodrug could be obtained, thanks the amphiphilic proterties of bile acids[4]. These conjugates showed significantly lower cytotoxicity toward normal cells while maintaining a good activity againts cancer cell lines. In orded to gain some insights into the mechanism of their action, a recently reported coumarine based fluorophore (Pacific blue[5]) has been liked to the 7-hydroxyl of the two conjugates **6** and **7**. The synthesis of the fluorophore-bearing conjugates required trying different routes but allowed, in the end, to obtain the two products in very high purifty after preparative RP-HPLC.

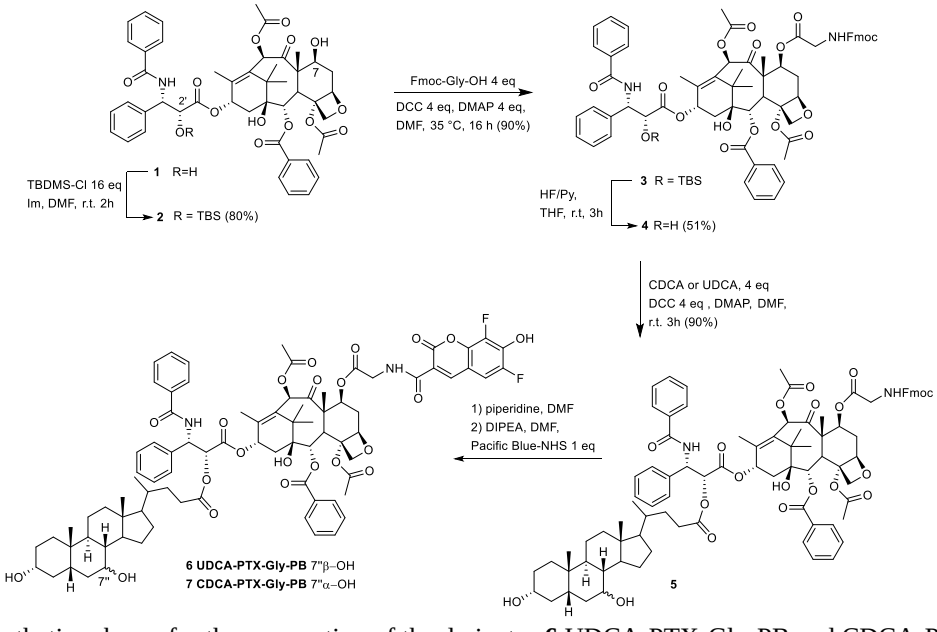

Figure 1. Synthetic scheme for the preparation of the derivates **6** UDCA-PTX-Gly-PB and CDCA-PTX-Gly-PB.

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P48 – LIPOSOMAL NANOVECTORS FOR THE DIAGNOSTIC USE OF MANGANESE: A PRELIMINARY TECHNOLOGICAL STUDY

Walter Pula,[a] Anna Bordin,[a] Anna Maran,[a] Maddalena Sguizzato,[a] Markus Drechsler,[b] Rita Cortesi,[a] Lorenza Marvelli [a]

[a] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Ferrara, Italy

[b] Bavarian Polymerinstitute (BPI), University of Bayreuth, Bayreuth, Germany

E-mail: pluwtr@unife.it

ABSTRACT

Recently, diagnostic imaging research has led to the development of multimodal imaging techniques such as positron emission tomography (PET) / magnetic resonance imaging (MRI) which allows to obtain at the same time metabolic information provided by PET and morphological information provided by MRI [1]. A fundamental prerequisite for obtaining a real fusion between the two imaging modalities is the use of chemically identical radioactive and paramagnetic contrast agent. In this regard, the transition metal manganese appears to be the ideal candidate as a potential bimodal contrast agent but due to its high dose toxicity, it is not currently used in diagnostics. In order to overcome toxicity problems, in the present study the production and characterization of anionic liposomes, as delivery systems for manganese were investigated.

Negatively charged liposomes were produced using the direct hydration method followed by extrusion [2]. Particularly, four different anionic surfactants were considered, namely sodium docusate, N-lauroylsarcosin sodium salt, Protelan AG8 and sodium lauroyl lactylate.

The obtained formulations were then characterized in terms of size, surface charge, efficiency of encapsulation and stability over time. The extruded liposomal dispersions are homogeneous and monodisperse with an average particle diameter not exceeding 200 nm. The measure of Z potential confirmed the presence of a negative surface charge. Preparations with N-lauroylsarcosin sodium salt and sodium lauroyl lactylate were considered to be the most stable over time and the presence of manganese did not affect their size distribution. Liposomal systems with Protelan AG8 and sodium docusate were instead excluded from the discussion due to their instability.

The two selected anionic liposomal systems were then tested for their in vitro antiproliferative effect on the human keratinocyte cell line (HaCaT) by MTT assay. The obtained results highlighted that both formulations are not toxic. Liposomes containing N-lauroylsarcosin sodium salt or sodium lauroyl lactylate were loaded with two manganese compounds with different water solubility.

The actual concentration of manganese in each formulation was determined by mean of atomic absorption spectroscopy demonstrating that the manganese compound with hydrophilic characteristics is retained almost completely within liposomes, whilst lipophilic manganese compound is loaded around the 60-70%. Moreover, these formulations showed a dose - dependent antiproliferative effect on HaCaT cell cultured in vitro.

Currently, the present study is still in progress with the aim of investigating the interaction between manganese and the negative charges of the surfactant and determining the magnetic properties of the obtained liposomal system, a relevant factor for the potential application in diagnostic imaging.

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P49 – A SIMPLE AND INDUSTRIALLY SCALABLE METHOD FOR MAKING A PANI-MODIFIED CELLULOSE TOUCH SENSOR

Ilaria Ragazzini,[a] Isacco Gualandi,[a] Serlio Selli,[b] Ciro Polizzi,[a] Maria Cristina Cassani,[a] Daniele Nanni,[a] Francesca Gambassi,[a] Fabrizio Tarterini,[a] Domenica Tonelli,[a] Erika Scavetta,[a] Barbara Ballarin [a]

[a] Department of Industrial Chemistry "Toso Montanari", Bologna University, Viale Risorgimento 4, I-40136, Bologna, Italy

[b] Cromatos s.r.l., via G. Cardano, 6B/C/D, 47122, Forlì, Italy

E-mail: ilaria.ragazzini6@unibo.it

ABSTRACT

Nowadays, alternatives to the traditional electronics that should be low cost, degradable, compostable and made from environmentally nontoxic substances are of great interest in research. As candidate, we propose bare fibers of cellulose made conductive by an in situ oxidative polymerization of aniline. The resulting composite fibers were employed to fabricate electroactive sheets using a pilot plant of a typical paper industry. The resistivity of the obtained sheets is 14 ± 1 Ω sq^{-1}, a value around 1000 times lower than those reported in literature. The higher electronic performances of the sheets were demonstrated by assembling a capacitive touch sensor device with optimized geometry. The touch sensor shows an increase of 3–4 % of the starting electric capacity after compression and a fast response time of 52 ms. To our knowledge this is the first time that a device is prepared in this way and therefore, the herein presented results can bring a significant improvement in the development of low-cost, green and high-tech electronic devices [1].

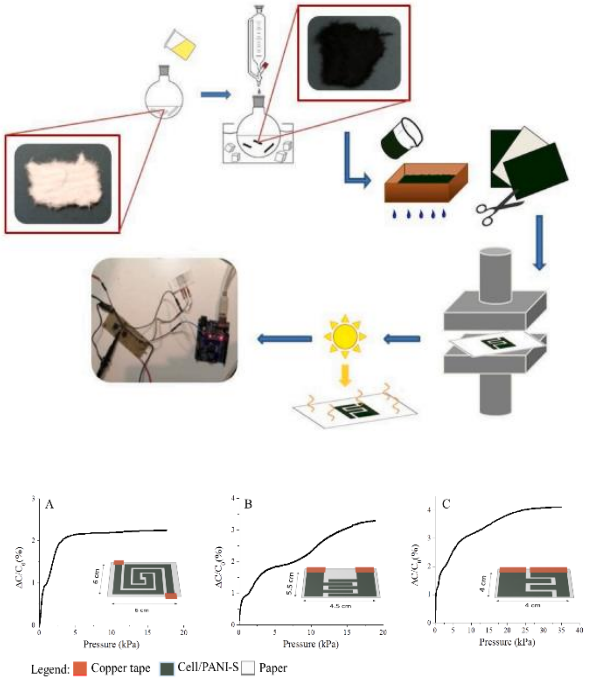

Figure 1. formation of the sensors and their response to pressure studies.

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P50 – THE IMPACT OF FLUORINE IN THE GELATION ABILITY OF A SHARED SCAFFOLD

Paolo Ravarino, Nadia Di Domenico, Demetra Giuri, Claudia Tomasini
Dipartimento di Chimica "Giacomo Ciamician", Alma Mater Studiorum Università di Bologna, Via Selmi 2, 40126, Bologna, Italy
E-mail: paolo.ravarino2@unibo.it

ABSTRACT

Low-molecular-weight (LMW) gelators are small molecules able to form gels, that are materials able to support their own weight when subjected to gravity. During the gelation process, the gelator molecules are firstly dissolved in a suitable medium, then after the addition of a trigger, they start to form fibres that entangle together and form the gel matrix.
It is possible to design new LMW gelators, following few guidelines. Among them, the insertion of moieties able to form weak bonds like H-bonds and hydrophobic interactions is a common strategy. However, predicting if a molecule can form a gel is not straightforward. Among all the possible weak interactions, π-π stacking plays a pivotal role in governing the gelation process [1]. As halogen atoms usually enhance π interactions and allow the formation of additional weak bonds [2], their insertion on aromatic rings is another strategy to improve the gelling ability of a molecule [3].
We studied three molecules, sharing the same scaffold with a different number of fluorine atoms on a phenyl ring (figure 1): Boc-^{D}Phe(F_n)-^{L}Oxd-OH (**F0**: n = 0; **F1**: n = 1; **F2**: n = 2). These molecules were tested for the formation of hydrogels under different conditions in EtOH:H_2O mixture in 3:7 ratio, in ^{i}PrOH:H_2O mixture in 3:7 ratio, in H_2O with GdL, and in H_2O with the addition of calcium ions.
Most of the gels display a broad range of transparency in the visible region. This property is very useful for optical and biomedical applications. The rheological properties and the morphology of these gels were analysed to compare the stiffness and the structure of the materials obtained.

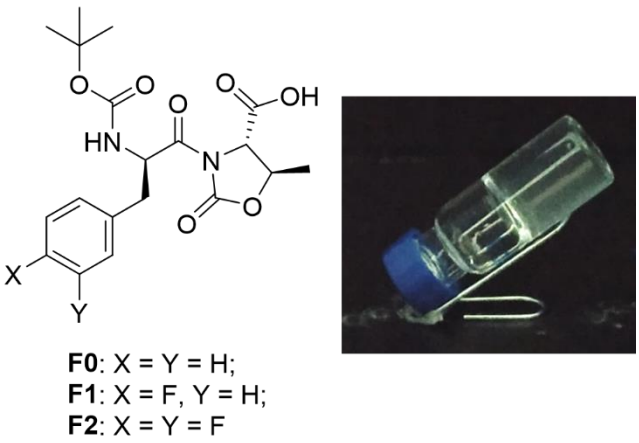

Figure 1. Left: molecular structure of the gelators synthesised; right: one of the gels formed.

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P51 – REALIZATION OF ELECTRICALLY RESPONSIVE NANOFIBERS FOR ARTIFICIAL MUSCLES

Mariangela Rea,[a] Carlo Gotti,[b] Andrea Zucchelli,[b] Francesca Soavi,[a] Catia Arbizzani,[a] Serena Silvi,[a] Alberto Credi,[c,d] Anna Liguori,[a] Chiara Gualandi,[a] Maria Letizia Focarete [a]
[a] Department of Chemistry "G.Ciamician", University of Bologna, Bologna, Italy
[b] Department of Industrial Engineering, University of Bologna, Bologna, Italy
[c] CNR_ISOF, Clan-Center for Light Activated Nanostructures, Bologna, Italy
[d] Department of Chemistry "Toso Montanari", Bologna, Italy
Email: mariangela.rea2@unibo.it

ABSTRACT

The development of artificial muscles to be employed in robotics is a challenging topic that is attracting increasing interest in the scientific community. An innovative strategy for the design of nanostructured electrically responsive materials for artificial muscles is represented by the incorporation of billions of artificial molecular machines inside polymeric electrospun nanofibers. These motor systems (Fig. 1b), represented by an electrically-activable polymer, can perform a linear contraction/extension movement at the single molecule level under electrical stimulation[1], mimicking the natural sliding mechanism occurring thanks to the alignment of actin and myosin filaments (Fig. 1a). Then, following a bottom-up approach, electrospun nanofibers can be assembled in hierarchical structures, in order to resemble the human skeletal muscles. By exploiting the coaxial electrospinning technique, core-shell nanofibers are developed, made of a conductive polymer as a core and a shell constituted by an elastomeric polymer, in which the artificial molecular machines are homogeneously dispersed and longitudinally aligned. A conductive coating is then deposited on the core-shell nanofibers, to guarantee the electrochemical activation of the molecular machines under an electrical stimulus[2]. Two main strategies were investigated for the realization of the coating: 1) dip coating in either conductive polymeric solution[3] or graphene dispersion; 2) electroless Cu plating[4]. All samples were thermally characterized and, mechanical tests coupled with resistance measurements were carried out, to assess fibers' electrical conductivity as a function of elongation. The aim of this work was to demonstrate that beads-free and aligned core-shell nanofibers can be obtained, to guarantee the electrical conductivity along the nanofiber axis and to demonstrate that molecular machines can be successfully electrospun inside the elastomeric carrier polymer.

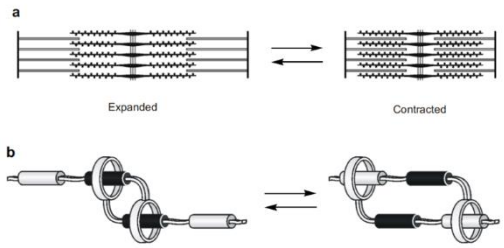

Figure 1. Expansion/contraction of a (a) natural muscle and (b) supramolecular electrically-activable polymer.

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ACKOWLEDGMENTS

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P52 – OPTIMING TEMOZOLOMIDE LOADING INTO HYBRID PLGA-CHOLESTEROL NANOPARTICLES FOR GLIOBLASTOMA MULTIFORME TREATMENT

Arianna Rinaldi,[a,b] Jason Thomas Duskey,[a] Riccardo Caraffi,[a] Giovanni Tosi,[a] Maria Angela Vandelli,[a] Barbara Ruozi [a]

[a] Nanotech Lab, Te.Far.T.I., Department. Life Sciences, University of Modena and Reggio Emilia, 41125, Modena, Italy; E-mail: arianna.rinaldi@unimore.it, barbara.ruozi@unimore.it

[b] Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, 41125, Modena, Italy

ABSTRACT

Glioblastoma multiforme (GBM) is the most aggressive and common malignant brain tumour, characterized by a life expectancy of only 12–18 months after diagnosis. Current treatments based on surgery, chemotherapy, and radiotherapy are not effective, resulting in a high rate of treatment failure and recurrences. [1] Temozolomide (TMZ) is an FDA approved DNA alkylating agent which is the the most effective and standard chemotherapeutic agent for GBM. The encapsulation of TMZ into nanocarriers allows increased bioavailability, enhanced accumulation at the tumour site, and decreased toxicity. [2] Despite all the efforts of using TMZ in nanomedicine, there are still numerous critical aspects related to TMZ-loaded nanoparticles that must be overcome: low encapsulation efficiency, failure in BBB crossing, low drug accumulation specifically in GBM cells, and low cellular uptake. Thus, novel nanotechnological approaches are urgently required to achieve more effective TMZ delivery to cancer cells. [3-5] The aim of this work was to develop a tailored nanomedicine for the delivery of Temozolomide to GBM cells. Hybrid nanoparticles composed by poly-(D,L-lactide-co-glycolide) polymer (PLGA) and Cholesterol (Chol), named (PLGA-Chol NPs), were investigated as potential platforms for the encapsulation of TMZ. Temozolomide-loaded PLGA-Chol NPs were formulated by using nanoprecipitation method, with the aim of optimizing TMZ loading into PLGA-Chol NPs by varying the formulation parameters (such as ratio between PLGA and Cholesterol, surfactant type and concentration, aqueous/organic phase ratio). After formulation, a physico-chemical characterization by Photon Correlation Spectroscopy (size, size distribution, surface potential), AFM images, and stability to preparation and storage were performed. Technological properties of encapsulation efficiency and loading content were also analysed. Optimized formulations exhibited a spherical shape with a size ≤300 nm and a low polydispersity index (≤0,3), with an Encapsulation Efficiency of approximately 36,0 % and a loading Content of 3,0 %. Future studies will focus on functionalizing PLGA-Chol NPs onto their surface with novel ligands selected to drive the developed nanomedicine in the Central Nervous System and selectively towards GBM cells. Optimization studies allowed the selection of the most proper formulation parameters, with the aim of developing a tailored nanomedicine as a new possibility for the treatment of one of the most difficult-to-treat tumors.

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This project was supported by MAECI grant (PI Tosi, Nanomedicine for BBB-crossing in CNS oncologic pathologies), IMI EU Grants Investigating Mechanisms and Models predictive of accessibility of therapeutics (IM2PACT) Into the Brain and "Mat2Rep" ER Project, Bando per progetti di ricerca industriale strategica rivolti agli ambiti prioritari della strategia di specializzazione intelligente" (DGR 986/2018) POR-FESR EMILIA ROMAGNA 2014-2020, Asse 1 – Ricerca e innovazione, Azione 1.2.2.

P53 – NOVEL LIGAND MODIFIED PLGA NANOPARTICLES FOR GLIOBLASTOMA MULTIFORME TARGETING

Arianna Rinaldi,[a,b] **Jason T. Duskey**,[a] **Ilaria Ottonelli**,[a,b] **Maura Samarani**,[c] **Ines Saenz de Santa Maria**,[c] **Maria Vittoria Grazioli**,[a] **Barbara Ruozi**,[a] **Maria Angela Vandelli**,[a,b] **Giovanni Tosi** [a]

[a] Nanotech Lab, Te.Far.T.I., Department. Life Sciences, University of Modena and Reggio Emilia, 41125, Modena, Italy; E-mail: arianna.rinaldi@unimore.it, gtosi@unimore.it

[b] Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, 41125, Modena, Italy.

[c] Unité de Trafic Membranaire et Pathogénèse, Département de Biologie Cellulaire et de l'Infection, Institut Pasteur, Paris, France

ABSTRACT

Nanoparticles (NPs) have gained increasing attention in the treatment of Glioblastoma Multiforme (GBM) to deliver therapeutics to the brain and provide selective targeting of the diseased cells, thus reducing adverse effects. However, therapeutic success of nanomedicines for GBM is hampered by several obstacles, including the presence of the blood-brain barrier (BBB), and the difficulty in selectively accumulating in the tumour site after reaching the brain. Moreover, once NPs reach the desired target, they can undergo intracellular trafficking via pathways such as transport via Tunneling Nanotubes (TNTs), whose formation is upregulated in cancer, making the fate of nanosystems often elusive and uncontrolled [1]. In this study, NPs based on the FDA approved polymer poly(lactic-co-glycolic) acid were surface modified with two ligands for BBB crossing, the Adeno-Associated Virus derived peptide PAAVF [2] and the glycopeptide g7 [3], and two ligands for GBM targeting, the monoclonal antibodies of the Cell Surface Vimentin (M08 and M08J), which is overexpressed in GBM cells [4]. First, formulation of NPs was optimized by varying some of the formulative parameters. Optimized NPs were fully characterized in terms of chemico-physical and morphological features. Then, targeting ability of the engineered NPs was evaluated *in vitro* on GBM cells (C6 cells). Further studies in a co-culture assay compared the cell-specific uptake and cell growth effects of targeted NPs on both GBM (C6) cells and healthy astrocytes (DITNC1). Optimized surface modified NPs showed a higher uptake *in vitro* than the non-modified ones. Co-culture assay showed not only a significantly higher uptake by GBM cells over healthy astrocytes for NPs conjugated with M08, but also an effect of M08-NPs in reducing GBM cell growth and promoting the growth of healthy astrocytes. Moreover, to assess the role of TNTs in NPs trafficking, a preliminary study on the interaction between NPs and TNTs was performed. M08-NPs and g7-NPs were incubated with CAD (neurons) and U251 (glioblastoma) cell lines. These studies demonstrated the uptake of targeted NPs by both cell lines, and remarkably that they were trafficked by TNTs. Overall, this study demonstrates the importance of proper surface modification of NPs to allow for targeted delivery to GBM.

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P54 – GREEN APPROACHES TO DESIGN AND SYNTHESIS OF POTENTIAL MULTIMERIC FAP SPECIFIC CHELATORS FOR THERANOSTIC APPLICATIONS

Chiara Roccatello,[a] Remo Guerrini,[a] Delia Preti,[a] Salvatore Pacifico,[a] Martina Fabbri,[a] Valentina Albanese,[a] Giovanni Paganelli [b]

[a] Department of Chemical Pharmaceutical and Agricultural Sciences, University of Ferrara, via L. Borsari 46, 44121 Ferrara, Italy. E-mail: chiara.roccatello@edu.unife.it

[b] Nuclear Medicine Unit (GP), Department of Medical Oncology (UDG), Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, Istituto di Ricovero e Cura a Carattere Scientifico (IRST) IRCCS, 47014 Meldola, Italy

ABSTRACT

Fibroblast Activation Protein α (FAP, FAP-α) is a membrane glycoprotein with an extensive extracellular domain which is upregulated in the tumor microenvironment of over 90% of epithelial cancers, while it is minimally expressed in healthy adult tissues.[1] For this reason, FAP is a strategic target for the development of radiopharmaceuticals with theranostic applications.

Hence, a new class of PET radiopharmaceuticals was synthesized by conjugating a DOTA chelating unit to two different FAP-selective inhibitors through a suitable spacer.[2] Preliminary studies about two molecules of that class (^{68}Ga-FAPI-2 and ^{68}Ga-FAPI-4) demonstrated a promising safety and efficacy profile as new radiotracers for non-invasive imaging. They also showed an optimal biodistribution, but a further increase of the residence time on the target is necessary to apply these compounds for both diagnostic and endoradiotherapeutic purposes, after conjugation with appropriate radionuclides such as ^{177}Lu, ^{90}Y or ^{225}Ac.[3] The research project aims to apply the molecular clustering technique known as Peptide Welding Technology (PWT) to increase the residence time of FAPI tracers on tumor tissues. It has been demonstrated that the conjugation of therapeutic agents on a central PWT core is an effective method to extend their duration of binding to the biological target.[4]

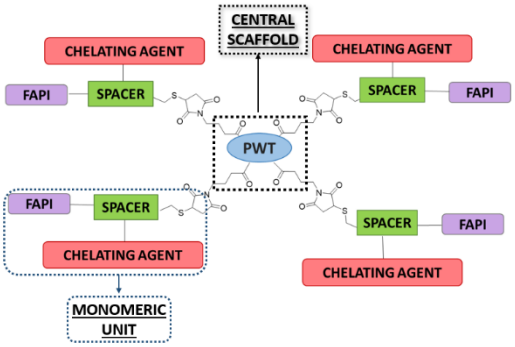

FIGURE 1. General structure of the molecular platforms.

It is planned to proceed with the liquid phase synthesis of the FAP-inhibiting portion of the molecules and the central core (PWT). Furthermore, a pseudopeptide spacer, synthesized via solid phase peptide synthesis approach (SPPS), will link the chelating portion to the FAP inhibitor. A thiol function will be inserted into the linker to conjugate the monomeric unit to the PWT tetramaleimide core via thiol-Michael reaction.

It is expected to apply a green approach to synthetize these compounds, mainly modifying the typical solid phase reaction conditions in favour of the use of more sustainable solvents, eventually assisted by microwaves or surfactants.[5] Furthermore the thiol-Michael reaction, used for the clusterization of the molecule, can be defined as "click" and "green" as it allows to conjugate a thiolate and an α,β-unsaturated carbonyl in mild reaction conditions and in aqueous environment.

The chelating ability and the biological profile of the synthesized molecules will be evaluated to identify the most promising compounds. The main aim of the project is to identify multimeric radiotracers with a longer lasting residence time on FAP, that will allow the development of new radiotherapy ligands for non-invasive diagnosis and treatment of various types of epithelial tumors.

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P55 – A CASE STUDY OF CO_2 AEROSOL REACTIONS: THE EFFICIENT CONVERSION OF STYRENE OXIDE TO CARBONATE IN MICRODROPLETS CONDITIONS

Caterina Rovegno,[a,b] Daniele Urbani,[a,b] Eleonora Polo,[a] Alessandro Massi,[b] Paolo Dambruoso [a]
Caterina Rovegno and Daniele Urbani equally contributed to this research.
[a] Institute for the Organic Synthesis and Photoreactivity of the Italian National Research Council, Area della Ricerca di Bologna, Via P. Gobetti, 101 – 40129 – Bologna (Italy)
[b] Department of Chemical, Pharmaceutical and Agricultural Sciences, University of Ferrara, Via L. Borsari, 46 – 44121 Ferrara (Italy)

ABSTRACT

Great attention has been recently paid by the scientific community to microdroplets reactions, because this innovative methodology can prompt a relevant acceleration [1] to valuable transformations. There are many reported examples of homogeneous liquid phase, and two phases liquid-liquid reactions in inert gas atmosphere that led to successful syntheses. The physical and physico-chemical phenomena which take place within the microdroplets or at their interface with gas are able to explain the obtained results [2]. Moreover, the promising results of the recently reported [3] water TPPS-mediated $^1O_2$ aerosol photochemical selective oxidation of sulfide to sulfoxide in air pave the way for the extension of this new approach to many biphasic gas-liquid transformations.
In this stimulating scenario we exploited this innovative paradigm to study the microdroplets conversion of styrene oxide to styrene carbonate in CO_2 atmosphere mediated by potassium iodide/triethylene glycol (KI/TEG) complex (Fig. 1).

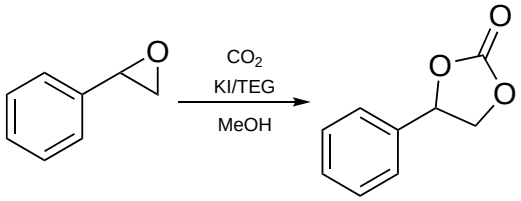

Figure 1: Scheme of the model reaction.

We herein present the study of this model reaction by comparing ordinary bulk *vs* microdroplets reaction at various temperatures and conditions, highlighting the positive effects of microdroplets conditions on reaction rates.

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P56 – DESIGN AND SYNTHESIS OF PEPTIDE-ZEOLITE MONOLAYERS FOR INFLAMMATORY PROCESSES CONTROL

Michele Anselmi,[a] Monica Baiula,[b] Federica Santino,[a] Junwei Zhao,[a] Santi Spampinato,[b] Natalia Calonghi,[b] Luca Gentilucci [a]

[a] Department of Chemistry "G. Ciamician", University of Bologna, via Selmi 2, 40126 Bologna, Italy; E-mail: michele.anselmi@iit.it, federica.santino2@unibo.it, juwzhao@ucdavis.edu, luca.gentilucci@unibo.it

[b] Department of Pharmacy and Biotechnology, University of Bologna, via Irnerio 48, 40126 Bologna, Italy; E-mail: monica.baiula@unibo.it, santi.spampinato@unibo.it, natalia.calonghi@unibo.it

ABSTRACT

Arg-Gly-Asp (RGD)-binding integrins, e.g., αvβ3, αvβ1, αvβ5 integrins, are currently regarded as privileged targets for the delivery of diagnostic and theranostic agents, especially in cancer treatment. In fact, integrins are one of the major families of adhesion receptors that mediate cell-cell and cell-extracellular matrix interactions. They are expressed on many cell types, and they are deeply involved in a variety of disease. Despite their great potential as target, most RGD antagonist gave contrasting results and repeatedly failed to demonstrate therapeutic benefits in cancer patient. Because of these reasons, recently, researchers focused on the alternative use of the RGD ligands as diagnostic devices. For this purpose, they have been conjugated to drugs, drug carrier systems, fluorescent tags, nanoparticles (NPs), materials, etc., for cancer therapy or imaging, and more recently for innovative applications, such as smart and responsive materials. In particular, α4β1 integrin is involved in inflammatory, allergic, and autoimmune diseases, therefore, it represents an interesting therapeutic target. Aiming at obtaining simple, highly stable ligands of α4β1 integrin, we designed hybrid α/β peptidomimetics carrying linkable side chains for the expedient functionalization of biomaterials, nano- and microparticles.

We identified the prototypic ligands MPU-PA-(R)-isoAsp(NHPr)-Gly-OH (12) and MPUPA-Dap(Ac)-Gly-OH (13) (MPUPA, methylphenylu-reaphenylacetic acid; Dap, 2,3-diamino propionic acid). Modification of 12 and 13 by introduction of flexible linkers at isoAsp or Dap gave 49 and 50, respectively, which allowed for coating with monolayers (ML) of flat zeolite crystals. The resulting peptide–zeolite MLs were able to capture selectively α4β1 integrin-expressing cells. In perspective, the α4β1 integrin ligands identified in this study can find applications for preparing biofunctionalized surfaces and diagnostic devices to control the progression of α4β1 integrin-correlated diseases. [1]

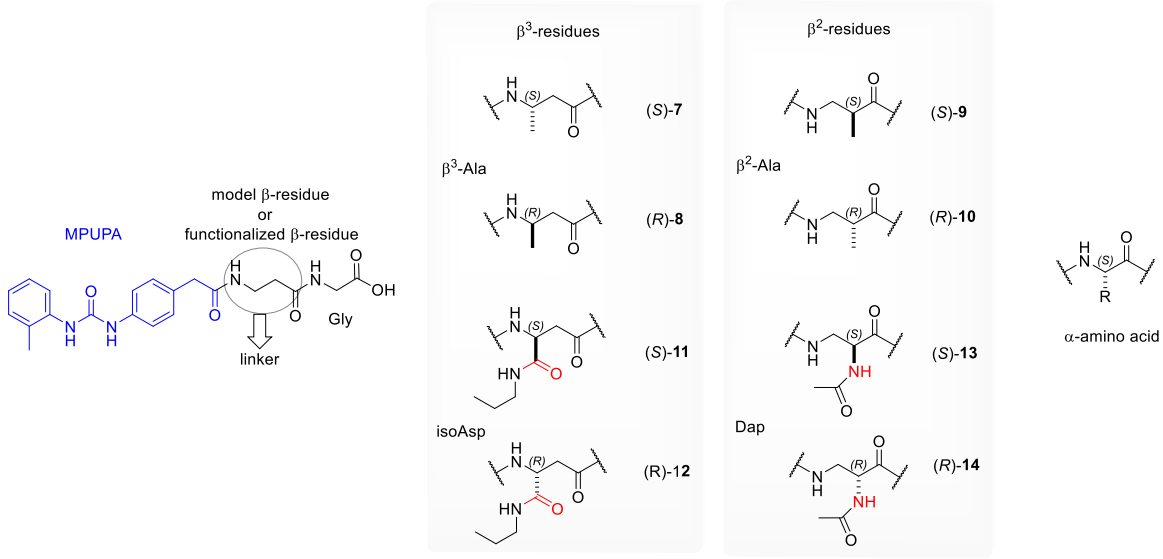

Figure 1. Sketches of candidate α4β1 integrin ligands 7-14 based on a hybrid α/β-peptidic structure

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P57 – ELECTROCHEMILUMINESCENT BIOSENSOR ON BDD ELECTRODE

Claudio Ignazio Santo,[a] Andrea Fiorani, [b] Yasuaki Einaga,[b] Giovanni Valenti, [a] Francesco Paolucci [a]
[a] Department of Chemistry "G. Ciamician", University of Bologna, Via Selmi 2, 40126 Bologna, Italy
[b] Department of Chemistry, Keio University 3-14-1 Hiyoshi, Yokohama 223-8522, Japan
E-mail: claudioignazio.santo@unibo.it

ABSTRACT

Biomarkers such as proteins, hormones, nucleic acids are biological indicators with a key role in identifying human body function variations. Electrochemiluminescence (ECL) became a leading technique in their detection for early diseases diagnosis, also thanks to high signal to noise ratio of the technique, due to the absence of a light source. ECL is a luminescent phenomenon generated by an electrochemical reaction [1]. In the commercial ECL-based immunoassays the biomarkers are detected after their immunorecognition through the creation of a labelled sandwich immunoassay attached onto magnetic microbeads. Beads are attracted to the working electrode surface using a magnet and ECL signal acquired after potential application (see scheme below). However, one of the main disadvantages of ECL in aqueous solutions is high potential necessary to produce light (typically 1.4 V), that could cause some modifications on the electrode surfaces (gold, platinum) and the generation of bubbles from water oxidation [2]. In the last years, few researchers focused their attention on the application of novel electrode materials in order to overcome those problems.
Herein, we will show the ECL application of Boron Doped Diamond electrode to beads-based immunoassay. BDD electrode exhibits superior properties, such as the fast reaction rate for the charge transfer reaction, wide potential window, low background current, high sensitivity, and high chemical stability. Thanks to its electrochemical stability, BDD allows to activate reactions that occur at high potentials without problems of the water oxidation [3]. It proved more suitable for ECL study at high oxidation potential.

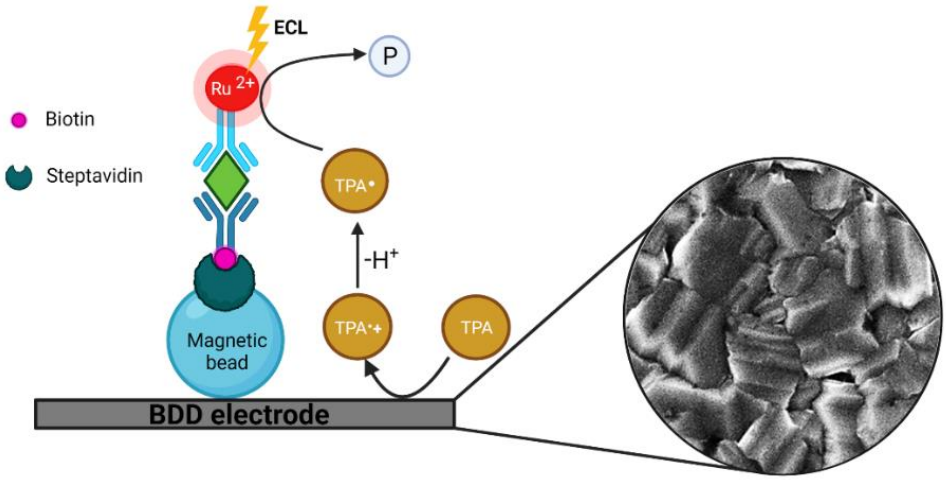

Figure 1. Schematic representation of bead-based electrochemiluminescent biosensor on BDD electrode

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P58 - BISMUTH COMPLEX OF QUINOLINE THIOSEMICARBAZONE RESTORES CARBAPENEM SENSITIVITY IN NDM-1-POSITIVE *Klebsiella pneumoniae*

Mirco Scaccaglia,[a] Martina Rega,[b] Cristina Bacci,[b] Franco Bisceglie,[a] Giorgio Pelosi [a]
[a] Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, 43124 Parma, Italy
[b] Department of Veterinary Sciences, University of Parma, Strada del Taglio 10, 43126 Parma, Italy

ABSTRACT

Resistant bacteria represent an urgent worldwide threat. The most used group of antibiotics is the class of beta-lactams thanks to their wide action spectrum on different bacterial families. As a common defense mechanism some microorganisms have developed a class of enzymes called beta-lactamases, able to hydrolyze the beta-lactam ring. Resistance to carbapenems, last resort antibiotics, is a major concern. Metal dependent beta lactamases (MBLs) are able to hydrolyze all the beta-lactam, including carbapenems.[1] To date no MBL inhibitors have been approved.
Metal-based compounds are getting more and more attention for their potential antibacterial activity.[2] Bismuth subcitrate can irreversibly inhibit MBLs via the displacement of the two active zinc(II) atoms with one bismuth(III) and represents a good scaffold for the development of large spectrum inhibitors of MBLs.[3] In this context, we have decided to expand the investigation to Bi(III) complexes.
Six bismuth complexes of general formula $BiLCl_2$, where L is a thiosemicarbazone bearing a quinoline moiety, have been synthesized and fully characterized, including their X-ray crystal structures. They have been studied in carbapenem resistant *Klebsiella pneumoniae* (NTCT14331) carrying the NDM-1 gene. The synergistic relationship between the compounds and meropenem have been studied in vitro. Quinoline-2-carboxaldehyde-N^4-phenyl-3-thiosemicarbazone bismuth dichloride showed an excellent synergism and could restore carbapenem sensitivity in the strain producing the NDM-1 enzyme. The minimum inhibitory concentration (MIC) of meropenem lowered down to 256 folds.

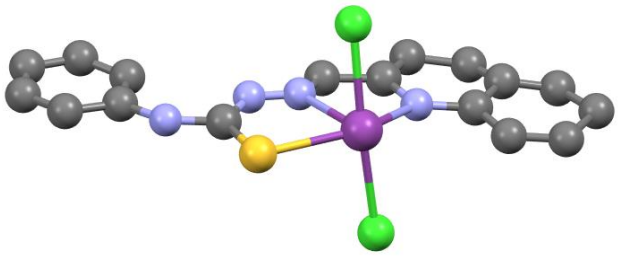

Figure 1. X-ray crystallographic structure of quinoline-2-carboxaldehyde-N^4-phenyl-3-thiosemicarbazone bismuth dichloride.

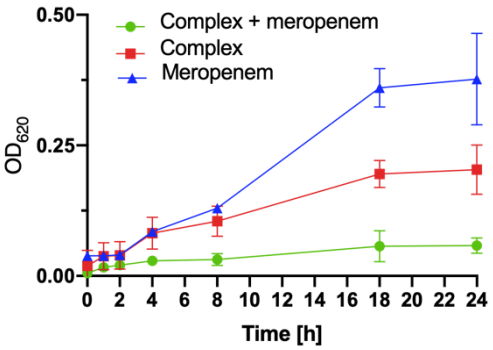

Figure 2. Time growth curves of meropenem (8 μgmL^{-1}) and quinoline-2-carboxaldehyde-N^4-phenyl-3-thiosemicarbazone bismuth dichloride (125 μM) monotherapy and in combination therapy against *K. pneumoniae* during 24h incubation.

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P59 – DESIGNING SELECTIVE CYS-LIGANDS TO UNPAIR THE BINDING OF THE HUMAN TRANSCRIPTION ENHANCER ASSOCIATED DOMAIN 4 (hTEAD-4) WITH ITS MODULATORS TO HALT CANCER CELL GROWTH

Lorenzo Tagliazucchi,[a] Giulia Malpezzi,[a] Cecilia Pozzi,[b] Ludovica Lopresti,[b] Alberto Venturelli,[a] Domenico d'Arca,[c] Gaetano Marverti,[c] Ciro Cecconi,[d] Glauco Ponterini,[a] Maria Paola Costi [a]

[a] Dept. of Life Sciences, University of Modena and Reggio Emilia, 41125 Modena, Italy
[b] Dept. of Biotechnology, Chemistry and Pharmacy, University of Siena, 53100 Siena, Italy
[c] Dept. of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia
[d] Dept of Physics, Informatics and Mathematics, University of Modena and Reggio Emilia

ABSTRACT

The Hippo Signalling cascade is an emerging target in tumour suppression regulation, neoplastic hypertrophy, and regenerative medicine. The pathway is activated by circulating anti-proliferative signals which leads to the phosphorylation of Yes Associated Protein (hYAP1) on Ser127/381, thus 14-3-3σ mediated cytosolic retention. Genetic alterations or exogenous factor may cause YAP nuclear migration and association to TEAD1-4 (Transcription Enhancer Associated Domain), triggering up-regulation of anti-apoptotic genes [1]. hTEAD is an enhancer that activates the nuclear transcription of genes as EMT's, EGFR and cyclins, and promotes the synthesis of survivin, tyrosine kinase HER3, and mitochondrial Bcl-xL involved in cell proliferation. TEAD binds a palmitic (palm) or myristic (myr) acids, tethered at Cys367 pocket, however its biological role is still not well known. hTEAD isoform-4 is the most represented of its family in solid tumours and its overexpression or mutation leads to cancer development and metastasis. Recent studies have considered hTEAD a promising target for anticancer drugs. Its inhibition strategy includes the disruption/prevention of YAP1:TEAD4 complex formation [2]. With the aim to develop a specific cysteine-directed inhibition strategy, we studied Cys on the protein surface and investigated their reactivity. Hence, our studies focus on characterizing the recombinant hTEAD4-ybd (aa217-434) surface though the analysis of the reactivity of its four Cys thiols (Cys310, Cys335, Cys367, Cys410), all close to YAP binding area. First, myr-Cys-367 was investigated to confirm the auto-myristoilation of the *E. coli* recombinant hTEAD4 through RP-chromatography on UHPLC-Orbitrap Q-Ex (ThermoFisher™) by multicharged TIC deconvolution, and the total myr-TEAD was assessed around 25%. Myristate position was confirmed by FASP protein tryptic hydrolysis and tandem-MS peptide analysis. We studied hTEAD binding of a small disulphides and thiols library with different chemical properties through the exposed cysteines residues in presence of different concentration of reducing agent [3]. Top8 DDA (HCD)-MS/MS scan on the tryptic peptides suggested the ligands' high selectivity towards Cys335. Cys367 was never found conjugated, even in the non-Myr fraction, hinting the low accessibility to the lipid pocket. The number of surface reactive Cys was confirmed by a reverse-titration of the protein against increasing amount of thiophenol; excess of unreacted thiophenol was measured by HPLC-UV-ELSD (Agilent™ 1260), suggesting a 1:1 stoichiometry. We confirmed hTEAD-ybd ligand ratio by fluoresceine labelling with absorption and fluorescence differential spectroscopy. The ongoing work engages the screening of a larger compound library to study YAP:TEAD interaction with a ligand displacement assay of labelled TEAD to a rhodamine-tagged peptidomimetic probe to achieve structural information of the heterodimer interface and to start a hit-optimization programme.

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P60 – APTAMERS AS BIORECEPTORS IN ANALYTICAL CHEMISTRY: A MULTITECHNICAL ASSESSMENT OF APTAMER-LYSOZYME INTERACTION POTENTIALITIES

Lorenzo Toma,[a] Monica Mattarozzi,[a] Francesco Grisenti,[a] Marco Giannetto,[a] Luca Ronda,[b] Valentina Marassi,[c] Pierpaolo Reschiglian,[c] Maria Careri [a]

[a] Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Italy

[b] Department of Medicine and Surgery, University of Parma, Italy

[c] Department of Chemistry, University of Bologna, Italy

E-mail: lorenzo.toma@unipr.it

ABSTRACT

Aptamers are single stranded DNA or RNA molecules gaining high attention in analytical chemistry as emerging recognition elements. Their sequence is selected by means of SELEX method, that would ensure high affinity for a particular target. Compared to antibodies, aptamers show several advantages, like easy and reproducible chemical synthesis, and simple modification for improved functionality. Although the notable amount of aptasensors and apta-assays devised up to now, challenges for practical and reliable application still remain, with particular attention to the effect of binding conditions and the behavior of negative control sequences [1].

The allergenic lysozyme from chicken egg white was selected as target for which several aptamers are reported in literature [2]; beyond anti-lysozyme aptamers, randomized sequences and PoliT were investigated as negative controls.

The initial scope of the work was the exploitation of aptamer-modified magnetic beads for the development of a competitive electrochemical magnetic apta-assay and an aptamer-based magnetic solid phase extraction (MSPE) method followed by LC-MS/MS analysis.

In order to study the experimental conditions influencing immobilized aptamer-lysozyme interaction, a simple electrochemical apta-assay was devised involving biotinylated lysozyme to directly assess the binding, investigating different blocking strategies and binding buffer. Unexpected results were obtained: negative controls and blank did not give signals significantly different from that obtained for anti-lysozyme aptamers. This evidence was confirmed by aptamer-based MSPE-LC-MS/MS analyses, thus raising some serious concerns about affinity and selectivity, and leading to a multi-technique study of aptamer-lysozyme interaction. Circular dichroism analysis has been made comparing spectra of 1:1 aptamer-lysozyme mixture and algebraic sum spectra of the two species in separated solutions; it was not possible to observe any conformational change, thus the asymmetry of system remains unchanged after Lys and aptamer mixing. Fluorescence titration was performed using a fixed concentration of lysozyme and varying aptamer concentration; binding curves were built and K_d values at µM level were extrapolated. The moderate affinity was also confirmed by Asymmetric Flow Field Flow Fractionation experiments.

The multianalytical platform clearly showed that anti-lysozyme aptamers are not suitable for target enrichment and pre-concentration and the binding to the target is not sequence specific [3]. This study invites to focus on the necessity to use negative control, to critically evaluate suitability of SELEX-selected aptamers for application in matrices as well as the necessity of a multi-technique approach to study aptamer-target interaction.

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P61 – SEPARATION AND RECYCLING OF CRITICAL METALS FROM MUNICIPAL AND INDUSTRIAL WASTE

Gianluca Torta, Fabrizio Passarini, Luca Ciacci, Ivano Vassura
Department of Industrial Chemistry "Toso Montanari", University of Bologna - Alma Mater Studiorum, Viale Risorgimento 4, 40136 - Bologna, Italy

ABSTRACT

Metals, in particular the platinum group metals (PGMs) and rare earth elements (REEs), are fundamental for modern technology as they provide essential properties to products such as permanent magnets, rechargeable batteries, catalysts, catalytic converters, superconductors, and similar. With these applications being expected to reduce energy consumption and mitigate the climate emergency, by extension REEs and PGMs can be relevant means for a transition to a greener society. However, the global demand for these strategical raw materials has increased dramatically in recent years. In Europe, a lack of natural deposits and negligible mine extraction make the EU Member States entirely dependent from imports to satisfy the domestic demand. Consequently, it has become an urgent priority to improve and enhance secondary resource supply (i.e., end-of-life products recovery and recycling) as a sustainable way of securing access to these elements. Recycling of metals from urban and industrial waste will make Europe less dependent from import as well as reduce waste disposal and environmental impacts, as recovery and recycling are generally less impacting than primary production.
However, one of the biggest issues with metal recycling is the relative low concentration of these elements in waste streams so that technological and economic issues are often the ultimate limit to a full industrial scale up. As a consequence, most of those critical metals for the European economy[1] are little recycled, if not entirely lost at end-of-life. In this view, this study aims at developing a recycling process for a set of strategic metals from urban and industrial waste. A preliminary selection of metals with significant recycling potentials includes lithium, nickel, cobalt from spent Li-ion batteries[2], neodymium, praseodymium, and dysprosium from permanent magnets[3], indium from liquid crystal displays[4], cerium, lanthanum, palladium, platinum, ruthenium, and gold from waste electrical and electronic equipment[5], and catalysts[6]. Starting from an extensive review of the most recent literature in this field, this work will evolve to focus on the setting of a strategy for the characterization of waste or by-products containing targeted metals. To this aim, innovative and emerging green recycling methods will be investigated, including metal leaching by means of ionic liquids and/or supercritical fluids for the identification, separation and purification of the elements or compounds of interest.

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P62 – CALIX[4]ARENE RECEPTORS FOR BACTERIAL STRAINS AND METABOLITES DETECTION

Carlo Alberto Vezzoni, Eloisa Tosi, Martina Polliotto, Laura Baldini, Francesco Sansone e Alessandro Casnati
Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco area delle Scienze 17/a, I-43124 Parma

ABSTRACT

The detection and quantification of bacteria species and their metabolites in human microbiota is a useful tool for the diagnosis of some pathologies and diseases, due to the symbiotic connection of human's health and bacteria's concentration in human body[1]. In the BacHound project a new approach is introduced to pursue this aim, using molecular and supramolecular receptors that interact with analytes through noncovalent interactions[2]. In this work we have synthetized three molecular receptors based on calix[4]arenes. In the first two cases the calix[4]arene scaffold bears hydroxyl groups at the lower rim to ensure the cone conformation and is functionalized at the upper rim with negative-charged sulfonate (**1**) or phosphonato (**2**) groups. The latter groups promote the interaction with polyamines, bacteria metabolites which result protonated at physiological pH. The third receptor (**3**) is a macrobicycle alkylated at the lower rim with hydrophilic ethoxyethyl groups and functionalized at the upper rim with a particular bridge able to recognize the terminal part of the peptidoglycan layer present on Gram positive bacteria cell wall. The receptors affinity with the targets has been studied through ^{1}H NMR titrations with different polyamines in the first two cases and with a model of peptidoglycan in the last case.

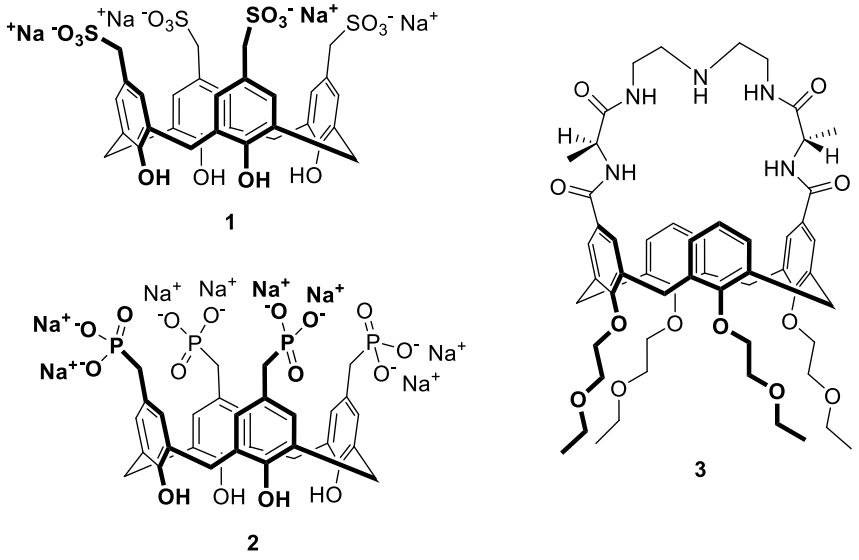

Figure 2. The three receptors presented in this work.

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P63 – FUNCTIONALIZED GOLD NANOPARTICLES AS AN ANCHOR TO DETECT COVID-19 INFECTION

Giulia Turrin,[a] Anna Fantinati,[b] Roberta Rizzo,[a] Sabrina Rizzo,[a] Erika Marzola,[a] Stefano Carli,[a] Claudio Trapella [a]

[a] Dept. of Chemical, Pharmaceutical and Agricultural Sciences, via Fossato di Mortara 17, 44121, Ferrara; E-mail: trrgli@unife.it

[b] Dept. of Environmental and Prevention Sciences, via Fossato di Mortara 17, 44121, Ferrara

ABSTRACT

The outbreak of a novel and highly pathogenic coronavirus (SARS-CoV-2) has presented a serious global public health emergency of coronavirus disease (Covid-19). During the first lockdown our team joined forces with several research areas trying to contribute to the emergency situation dictated by the Covid-19 pandemic. We focused our interest on diagnostics, given the critical issues highlighted by the swab tests processed with RT-PCR technique (costs, time, need for specialized personnel). The aim of our project was to develop a smart, rapid and sensitive method to detect a current SARS-CoV-2 infection in individuals, a device that is affordable for everyone. The virus detection system initially involves the functionalization of gold nanoparticles (GNPs) with a specific peptide portion of ACE-2, the human protein that is essential for the infection to occur. These gold nanoparticles must pass through an electronic device developed by engineers of Elements s.r.l in Cesena, Italy. This tool is characterized by a nanometer-sized pore through which flows an electric current. At this point, a sample of patient's spit is mixed together with the suspension of functionalized beeds: if the patient is affected by Covid-19 infection, a slowing down or an interruption of the current passage will be detected. This happens because the functionalized GNPs act as an anchor and bind strictly and specifically the Receptor-Binding Domain (RBD) of the virus. Gold particles of known size and commercially available were functionalized by exploiting gold's high affinity for sulfur to form the thioauric bond [1]. Using the solid-phase peptide synthesis (SPPS), various peptide aptamers of the ACE-2 protein were synthetized to evaluated which one showed the best activity in interacting with RBD. All peptides were modified by adding to the N-terminal domain a cysteine, which is permissive to obtain the Au-S bond. The best sequence combination is characterized by 19 amino acids: H-Gln-Ala-Lys-Thr-Phe-Asp-Lys-Phe-Asn-His-Glu-Ala-Glu-Asp-Leu-Phe-Tyr-Gln-Cys-NH_2 [2]. Gold nanoparticles were functionalized with both the peptide and the zwitterion Sulfobetaine-Thiol (SB-Thiol), to avoid the formation of particles agglomeration (Figure 1).

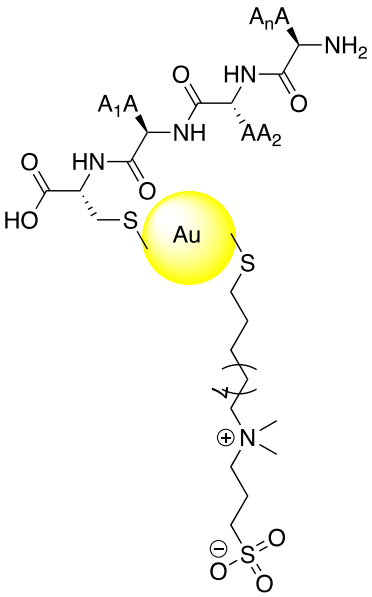

Figure 1. Simplified structure of functionalized gold nanoparticle

The confirmation of the GNPs functionalization was given by the X-Ray photoelectron spectroscopy (XPS) (thanks to the IIT, Genova, Italy) and by immunofluorescence essays (thanks to the section of Microbiology, University of Ferrara, Italy). To date, we can say that the first part of the project has been developed, but since this is an early and multidisciplinary project, many aspects still need to be refined. The future perspectives will be therefore to improve the diagnostic system and also to make tests using the human SARS-CoV-2 in the high security laboratory BSL-3 of the University of Ferrara.

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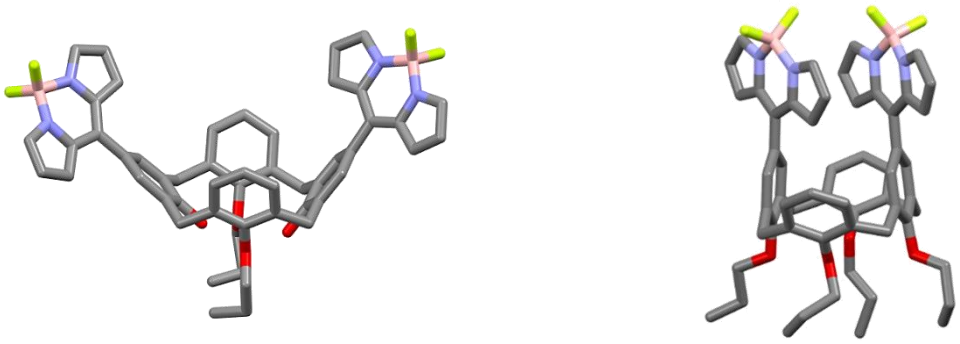
P64 – FINE TUNING THE INTERACTIONS BETWEEN BODIPY DYES SUPPORTED ON A CALIX[4]ARENE

Lucia Visieri, Laura Baldini
Dipartimento di Scienze Chimiche, della Vita e della Sostenibilità Ambientale, Università di Parma, Parco area delle Scienze 17/a, I-43124 Parma

ABSTRACT

The calix[4]arene scaffold in the *cone* conformation provides an ideal platform to study the interactions between groups present at its upper rim. The residual flexibility of the macrocycle, in fact, can be finely controlled by the appropriate functionalization of the lower rim. In this work, we compare the spectral properties of two calix[4]arenes (**1** and **2**) identically functionalized at the upper rim with two BODIPY dyes, but differing for the number of propyl chains present at the lower rim.
When only two propyl chains are present (compound **1**), two strong hydrogen bonds between the free OHs and the neighbouring phenol oxygen atoms rigidify the scaffold in a *regular cone* structure and, therefore, the two dyes are held far apart.[2] The UV-vis absorption and emission spectra of **1** are indeed typical of a monomeric BODIPY.
On the contrary, the four propyl chains of compound **2** allow a residual conformational mobility of the aromatic rings[1] that are free to oscillate back and forth. Without the hydrogen bonds, the system adopts a *pinched cone* geometry in consequence of attractive π–π interactions between the dyes. The emission spectra of **2** are thus characterized by an excimer-like band shifted to longer wavelengths.
We are currently investigating if the effect of an external force or stimulus on calixarene **1** could overcome the hydrogen bonds and push the two chromophores in close proximity, aiming to restore the excimer formation.



1 **2**

Figure 1. Solid state structures of the target compounds of this work.

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P65 – RATIONAL DRUG DESIGN AND SYNTHESIS OF TRYPANOTHIONE REDUCTASE INHIBITORS FOR TARGETING LEISHMANIASIS

Eleonora Testi, Alessandra Salerno, Riccardo Ocello, Matteo Masetti, Maria Laura Bolognesi
Department of Pharmacy and Biotechnology, Alma Mater Studiorum - University of Bologna, Via Belmeloro 6, 40126, Bologna, Italy
E-mail: eleonora.testi4@unibo.it

ABSTRACT

Species of the genus *Leishmania* (Kinetoplastida, Trypanosomatidae) are the causative organisms of leishmaniasis, a neglected tropical disease for whom only a small number of drugs exist, with poor safety, efficacy, and pharmacokinetic profiles. The most severe form of leishmaniasis is the visceral one which is the one responsible for causing substantial health problems in up to 400,000 people and up to 40,000 deaths per year and nowadays is spreading in new areas like Mediterranean basin, including Italy, so new therapeutic modalities are thus needed.[1]
Leishmania spp. possess a peculiar and specific redox metabolism that is based on the low molecular mass dithiol trypanothione [bis(glutathionyl) spermidine [T(SH)2] and trypanothione reductase (TR) - which keeps it in the reduced form. This enzyme is nowadays considered as one of the best possible targets in pursuing antitrypanosomatid drugs since TR is (i) absent in the human host; (ii) essential and validated for parasite survival (iii) available as the 3D structure.[2]
Numerous compounds of varied chemical nature have been tested as potential antileishmanial agents. Among them, phenothiazines, a group of tricyclic neuroleptic compounds traditionally employed as antidepressant, anxiolytic and antipsychotic, are particularly interesting.[3]
In this work, we reported a theoretical docking study conducted on a set of previously reported *Leishmania* Trypanothione Reductase (TR) inhibitors. Computer-aided drug design methods and molecular modelling techniques were applied in order to elucidate the best binding mode of tricyclic compounds at TR active site while retaining their inhibition activity. Molecular Dynamics simulations were also carried out for the best-ranked energy score compounds and comparisons were made regarding similar studies performed previously on TR inhibitors.
This comprehensive study on TR binding site has allowed (i) the detection of the fundamental interactions and analysis of the new "*3 points attack*" binding mode; (ii) the hypothesis of a SAR; (iii) the evaluation of a potential linker insertion for compound derivatization.
Finally, the best energy scored molecules were synthesized and evaluated for TR binding and inhibition activity and phenotypical antileishmanial efficacy.
Overall, this work has laid the foundation to streamline the TR inhibitors development pipeline from *in silico* to biological evaluation.

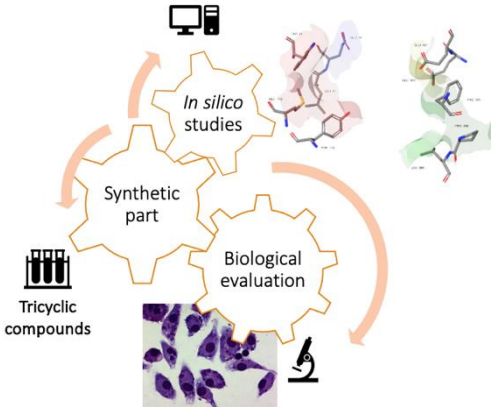

Figure 1. TR inhibitors development pipeline

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