UNIVERSITÁ DEGLI STUDI DI TERAMO

Società Chimica Italiana
Sezione Abruzzo

XXXV TUMA 2016

CONGRESSO DELLE SEZIONI TOSCANA-UMBRIA-MARCHE-ABRUZZO
DELLA SOCIETÀ CHIMICA ITALIANA

GIULIANOVA, 25-27 SETTEMBRE 2016

TUMA 2016
TOSCANA UMBRIA MARCHE ABRUZZO

XXXV Congresso
delle Sezioni
Toscana-Umbria-Marche-Abruzzo
della Società Chimica Italiana

TUMA 2016

Giulianova 25, 26 e 27 settembre 2016

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Benvenuti al XXXV Congresso della Società Chimica Italiana - Sezione Abruzzo

La sezione Abruzzo della Società Chimica Italiana è lieta di invitare i colleghi impegnati nella ricerca in tutte le discipline della Chimica a partecipare al XXXV Convegno - TUMA2016, che si svolgerà a Giulianova, presso L'Hotel Cristallo, dal 25 al 27 Settembre 2016.

Sarà una grande occasione per potersi confrontare su temi comuni e ascoltare dalla viva voce dei protagonisti lo stato attuale della ricerca in molti campi della chimica. Il Convegno sarà anche occasione per i giovani ricercatori di presentare i risultati del proprio lavoro, per questo abbiamo il piacere di bandire quattro borse di studio per la partecipazione di giovani ricercatori non strutturati.

Si ringraziano:

Dompé farmaceutici

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			9:45	10:15	**CP2 - Martellini KyN**	10:15	10:35	**CO13 - Carta**
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CB 10 minuti
CO 20 minuti
CP 30 minuti
PL 45 minuti

XXXV TUMA 2016

25-27 Settembre 2016

Hotel Cristallo Giulianova (TE)

PROGRAMMA

Domenica 25 Settembre 2016

12:00-14:30 **Cocktail di Benvenuto – Registrazione dei partecipanti**

14:30-15:00 **Apertura del convegno e saluto delle autorità**

15:00-16:55 **Sessione 1 –** Presiede **Antonella Fontana**

15:00-15:45 **PL1 – Alessandra Tolomelli**
Dipartimento di Chimica "G. Ciamician", Università di Bologna
"Linear and cyclic dehydro-b-amino acid as scaffolds for the synthesis of RGD-mimetics: from integrin ligands to delivery systems"

15:45-16:15 **CP1 – Adriano Mollica**
Dipartimento di Farmacia, Università "G. d'Annunzio" di Chieti Pescara
"Progettazione di peptidi ciclici agonisti misti μ/δ oppioidi"

16:15-16:25 **CB1 – Corinne Dalila Paoletti**
Scuola di Scienze del Farmaco e dei Prodotti della Salute, Università di Camerino
"Il 77-LH-28-1 come modello nella progettazione e sintesi di nuovi ligandi per i recettori D_2-like della dopamina"

16:25-16:35 **CB2 – Piera Eusepi**
Dipartimento di Farmacia, Università "G. d'Annunzio" di Chieti Pescara
"Prodrugs solubili del carvacrolo a potenziale attività antibatterica"

16:35-16:45 **CB3 – Valentino Canale**
Dipartimento di Farmacia, Università "G. d'Annunzio" di Chieti Pescara
"Separation of CO_2 and CH_4 from biogas by forming chemically promoted clathrate hydrates"

16:45-16:55 **CB4 – Valeria Ettorre**
Dipartimento di Farmacia, Università "G. d'Annunzio" di Chieti Pescara
"Produzione e caratterizzazione di network 3D a base di grafene"

16:55-17:10 **Pausa –** Coffee Break

17:10-19:10 **Sessione 2 –** Presiede **Francesco De Angelis**

17:10-17:30 **CO1 – Pasquale Linciano**
Dipartimento di Scienze Farmaceutiche, Università degli Studi di Modena e Reggio Emilia
"Fragment-based drug discovery applied to Trypanosoma brucei PTR1. discovery of two lead series with high ligand efficiency"

17:30-17:50 **CO2 – Matteo Santucci**
Dipartimento di Scienze della Vita, Università degli Studi di Modena e Reggio Emilia
"Difunctional folic acid-octapeptide bioconjugate engineering to intracellular trafficking anticancer target"

17:50-18:10 **CO3 – Fanì**
Dompé Farmaceutici spa
"Ritenzione di configurazione nella sintesi, via microonde, di bioisosteri 1H-tetrazolici chirali da derivati fenil propionici"

18:10-18:20 **CB5 – Luana Del Vecchio**
Dipartimento di Scienze Fisiche e Chimiche, Università dell'Aquila
"Synthesis of Oxazolidinone Derivatives from Propargylic Carbamates"

18:20-18:40 **CO4 – Elisabetta Rossi**
Dipartimento di Scienze Farmaceutiche, Sezione di Chimica Generale e Organica "A. Marchesini", Università degli Studi di Milano
"Gold(I) and Gold(III) catalyzed cycloaddition/cyclization reactions of vinylindoles with allenes"

18:40-19:00 **CO5 – Manuela Stefanelli**
Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma Tor Vergata
"Efficient Synthetic Methodologies to Extend the Corrole Ring Conjugation"

Lunedì 26 Settembre 2016

8:45-10:55 **Sessione 3**
dedicata a **Pietro Mazzeo**
già Professore Ordinario di Chimica Analitica
Università degli Studi dell'Aquila

Presiede **Angelo Antonio D'Archivio**

08:45-09:30 **PL2 – Francesco Ricci**
Dipartimento di Scienze e Tecnologie Chimiche, Università di Roma, Tor Vergata
"Nature inspired DNA based sensors and nanomachines"

9:30-9:45 **CO – Giuseppe Carlucci**
Dipartimento di Farmacia, Università "G. d'Annunzio" di Chieti-Pescara
"Un ricordo di Piero Mazzeo"

9:45-10:15 **CP2 – Tania Martellini**
Dipartimento di Chimica "Ugo Schiff", Università di Firenze
KeyNote *"Polybrominated diphenyl ethers (PBDEs) in the environment: Source and Environmental fate"*

10:15-10:35 **CO6 – Salvatore Milone**
Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise "G. Caporale"
"Legame con il territorio di origine di caciocavalli molisani: studio tramite approccio "untargeted" in spettroscopia ^{1}H-HR-NMR"

10:35-10:55 **CO7 – Maria Maggi**
Hortus Novus, L'Aquila
"Geographical classification of saffron (Crocus sativus L.) by linear discriminant analysis applied to the UV-Visible spectra of aqueous extracts"

10.55-11:10 **Pausa –** Coffee Break

11:10-13:20 **Sessione 4 –** Presiede **Giorgio Cerichelli**

11:10-11:30 **CO8 – Marcello Locatelli**
Dipartimento di Farmacia, Università "G. d'Annunzio" di Chieti-Pescara
"Il MAE, UAE ed estrazione convenzionale di composti bioattivi in radici di Pueraria lobata e valutazione della loro attività inibitoria su isoforme di anidrasi carbonica"

11:30-11:50 **CO9 – Martina Maya Cecchini**
Dipartimento di Scienze Fisiche e Chimiche, Università degli Studi dell'Aquila
"Electrospray ionization mass spectrometry: a fascinating tool for exploring the structure of poly(ionic liquid)s"

11:50-12:10 **CO10 – Flavio Della Pelle**
Department of Analytical Chemistry, Physical Chemistry and Chemical Engineering, Faculty of Biology, Environmental Sciences and Chemistry, University of Alcalá
"Press-Transferred carbon black nanoparticles: a new exclusive transducer for electrochemical sensing"

12:10-12:20 **CB6 – Marika Pellegrini**
Facoltà di Bioscienze e tecnologie agro-alimentari e ambientali, Università di Teramo
"The bioactive compounds of Abruzzo's officinal plants: extraction and chemical investigations"

12:20-12:30 **CB7 – Maria Chiara Boarelli**
School of Science and Technology, Chemistry Division, University of Camerino
"SPME-GC-MS to analyze volatile organic compounds produced during cooking"

12:30-12:50 **CO11 – Elisabetta Troni**
Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia
"Influence of preparation conditions on structural and mechanical properties of SPEEK membranes for PEMFCs"

12:50-13:10 **CO12 – Marika Marinelli**
Scuola di scienze e tecnologie, Divisione Chimica, Università di Camerino
"Additivi inorganici ritardanti di fiamma non alogenati: idrossido di magnesio naturale ed idrossido di alluminio prodotti per macinazione"

13:10-13:20 **CB8 – Roberto D'Amato**
Dipartimento di Chimica, Biologia e Biotecnologie, Università di Perugia
"Cerium oxide particles functionalized with phosphonic acids for radical scavenging use in PEMFC"

13:30-14:30 **Pranzo -** *Light lunch Buffet*

14.00-16:00 **Sessione Poster**

16.15 Partenza per la **Gita Sociale**

17:00 Arrivo a **Civitella del Tronto**

17:15 Visita guidata alla **Fortezza Borbonica di Civitella del Tronto** (durata circa 1 ora)

20:00 Cena Sociale presso **Ristorante Zunica 1880**

Martedì 27 Settembre

9:00-11:15 **Sessione 5 –** Presiede **Elisabetta Rossi**

09:00-09:45 **PL3 – Silvia Giordani**
Nano Carbon Materials Research Lab at the Italian Institute of Technology in Genova
"Functionalized carbon nanomaterials for biomedical applications"

09:45-10:15 **CP3 – Giuseppe Manfroni**
Dipartimento di Scienze Farmaceutiche, Università degli Studi di Perugia
KeyNote *"Identification, hit explosion, and mechanism of action investigation of pyridobenzothiazoles as anti-flavivirus compounds"*

10:15-10:35 **CO13 – Fabrizio Carta**
Dipartimento NEUROFARBA, Sezione di Farmacologia, Università degli Studi di Firenze
"From Dithio to Monothiocarbamates: New carbonic Anhydrases Inhibitors Possessing Intraocular Pressure Lowering Activity"

10:35-10:45 **CB9 – Gianmarco Ghiandoni**
Dipartimento di Scienze Farmaceutiche, Università degli Studi di Perugia
"Design, synthesis and biological evaluation of new pyrazolobenzothiazine analogues as p38α MAPK inhibitors"

10:45-11:15 **CP4 – Matteo Tiecco**
Dipartimento di Chimica, Biologia e Biotecnologie, Università degli Studi di Perugia
"Novel zwitterionic deep eutectic solvents: characterizations and synthetic applications"

11:15-11:30 **Pausa –** Coffee Break

11:30-13:05 **Sessione 6 –** Presiede **Dario Compagnone**

11:30-11:50 **CO14 – Francesca Di Renzo**
Department of Physical and Chemical Sciences, University of L'Aquila
"Reusability of Chloroperoxidase immobilized on polysaccharide-coated magnetic nanocapsules"

11:50-12:10 **CO15 – Gabriella Giulia Pulcini**
Scuola di Bioscienze e Medicina Veterinaria, Università degli Studi di Camerino
"E-learning e Stili di Apprendimento a supporto della chimica"

12:10-12:20 **CB10 – Michele Ciulla**
Dipartimento di Farmacia, Università "G. d'Annunzio" di Chieti-Pescara
"Peptidi inibitori del quorum sensing incapsulati in nanoparticelle polimeriche per l'eradicazione del biofilm da S. aureus"

12:20-12:30 **CB11 – Issam Abdalghani**
Department of Physical and Chemical Sciences, University of L'Aquila
"Study of the catalytic activity of cis-dioxomolybdenum(VI) catalysts bearing α-aminoacid ligands, for mild and selective oxyfunctionalization of olefins"

12:30-12:40 **CB12 – Cristina Minnelli**
Dipartimento Di.S.V.A. Università Politecnica delle Marche
"Liposomi funzionalizzati con mannosio-6-fosfato come Targeted Delivery Systems (TDS)"

12:40-12:50 **CB13 – Grazia Leonzio**
Dipartimento Di Ingegneria Industriale Dell'Informazione e Di Economia, Università dell'Aquila
"Analisi fluidodinamica di digestori anaerobici"

12:50-13:05 **CO16 – Marco Chiarini**
Facoltà di Bioscienze e tecnologie agro-alimentari e ambientali, Università di Teramo
"Magnetic Resonance techniques powerful tools for antioxidant activity investigation in supramolecular assemblies"

13.05-13.15 **Chiusura del Convegno**

COMUNICAZIONI ORALI

IL 77-LH-28-1 COME MODELLO NELLA PROGETTAZIONE E SINTESI DI NUOVI LIGANDI PER I RECETTORI D_2-LIKE DELLA DOPAMINA

Corinne Dalila Paoletti, Fabio Del Bello, Mario Giannella,

Alessandro Piergentili, Wilma Quaglia

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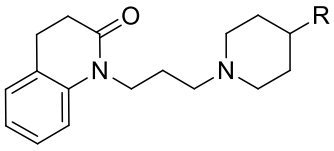
I recettori muscarinici M_1 dell'acetilcolina rappresentano un bersaglio attraente per il trattamento dei deficit cognitivi associati a malattie come il morbo di Alzheimer e la schizofrenia. Tuttavia, la scoperta di agonisti sottotipo-selettivi è stata ostacolata dall'alto grado di conservazione del sito di legame ortosterico dell'acetilcolina tra i sottotipi muscarinici M_1-M_5. L'avvento dei test di screening funzionali ha permesso l'identificazione di agonisti, come il 77-LH-28-1, che si legano a un sito allosterico e attivano selettivamente il sottotipo M_1. Tuttavia il 77-LH-28-1 mostra anche affinità per il sottotipo recettoriale D_2 della dopamina (D_2R).[1] La sottofamiglia D_2-like comprende i sottotipi D_2R, D_3R e D_4R, ciascuno dei quali riduce la produzione di cAMP e regola l'attività di vari canali ionici. L'ampia espressione dei recettori D_2-like nel sistema nervoso centrale e la modulazione di diversi processi neurologici, tra cui la gratificazione, la cognizione, l'apprendimento e la memoria, li rendono attrattivi bersagli farmacologici.[2] Pertanto, per ottenere maggiori informazioni sulle proprietà farmacologiche del 77-LH-28-1 sui recettori dopaminergici, è stata valutata l'affinità di questo composto per i sottotipi dei recettori D_2-like mediante spiazzamento del radioligando [^{3}H]N-metilspiperone in membrane ottenute da cellule HEK293 che esprimono stabilmente i sottotipi D_2R, D_3R e D_4R umani. Sorprendentemente, il composto 77-LH-28-1 ha evidenziato un'alta affinità per il D_4R e significativa selettività rispetto al D_2R e al D_3R. Per meglio comprendere le caratteristiche strutturali necessarie per l'interazione selettiva con il D_4R, sono stati sintetizzati nuovi derivati del 77-LH-28-1 in cui la catena alifatica butilica è stata sostituita con catene alifatiche e aromatiche di diversa lunghezza (Figura 1).



77-LH-28-1, R = $(CH_2)_3CH_3$

1: R = CH_3
2: R = $(CH_2)_2CH_3$
3: R = $(CH_2)_4CH_3$
4: R = C_6H_5
5: R = $CH_2C_6H_5$
6: R = $(CH_2)_2C_6H_5$
7: R = $(CH_2)_2CH_2OH$
8: R = $(CH_2)_4CH_2OH$
9: R = $(CH_2)_6CH_2OH$
10: R = $(CH_2)_8CH_2OH$
11: R = $(CH_2)_{10}CH_2OH$
12: R = $(CH_2)_{12}CH_2OH$

Figura 1

I nuovi derivati sono stati saggiati sia sui sottotipi D_2R, D_3R e D_4R, che sui 5 sottotipi muscarinici M_1-M_5, allo scopo di valutare le differenze strutturali tra questi sistemi e di ottenere agenti selettivi per il recettore D_4, potenzialmente utili per il trattamento della dipendenza da sostanze d'abuso.[3] I risultati dei saggi biologici dei nuovi derivati verranno illustrati nel corso della presentazione.

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[2] Zhang, A.; Neumeyer, J. L.; Baldessarini, R. J.; *Chem. Rev*. **2007**, *107*, 274-302.
[3] Yan, Y.; Pushparaj, A.; Le Strat, Y.; Gamaleddin, I.; Barnes, C.; Justinova, Z.; Goldberg, S. R.; Le Foll, B. *Neuropsychopharmacology* **2012**, *37*, 685-696.

PRODRUGS SOLUBILI DEL CARVACROLO A POTENZIALE ATTIVITÀ ANTIBATTERICA

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Negli ultimi anni, il Carvacrolo (2-metil-5-[1-metiletil]fenolo), un costituente degli olii essenziali di numerose piante appartenenti alla famiglia delle Labiatee, ha suscitato notevole interesse per le sue proprietà antibatteriche, fungicide ed antitumorali. Sono stati proposti due differenti meccanismi d'azione attraverso i quali spiegare come il Carvacrolo possa esercitare la sua attività antimicrobica, soprattutto nei confronti dei batteri Gram positivi. In primo luogo, il monoterpene destabilizza la membrana batterica generando un flusso di ioni H^+ verso l'interno della cellula responsabile della riduzione del potenziale di membrana e, quindi, del gradiente di pH. In secondo luogo, intercalandosi tra i fosfolipidi, altera le frazioni lipidiche della membrana citoplasmatica batterica. La presenza del gruppo idrossilico e del sistema aromatico sono i requisiti strutturali fondamentali responsabili di tali attività.[1,2]

Tuttavia, l'elevata lipofilia (LogP = 3.64) e la bassa solubilità in acqua (0.11 mg/mL) non consentono un adeguato assorbimento orale riducendo in tal modo la sua efficacia terapeutica. Uno dei principali approcci per superare tali inconvenienti è convertire composti insolubili in acqua in prodrugs mediante il legame covalente di una specifica porzione in grado di aumentarne la solubilità. Il presupposto dell'impiego dei profarmaci è che il legame tra il farmaco originatore e la porzione idrofila sia bioreversibile.[3]

Lo scopo di tale studio è stato quello di sintetizzare nuovi prodrugs (**WSCP1-17**) del Carvacrolo solubili in acqua mediante il legame di idonei linkers che, in condizioni fisiologiche, possono rilasciare spontaneamente il monoterpene mediante ciclizzazione intramolecolare con conseguente formazione di una imide. In particolare, gruppi funzionali idrofilici (aminoacidi naturali) e spacers "self-cleavable" (catene glutariliche e succiniche) sono stati coniugati alla molecola di Carvacrolo.

Le analisi delle proprietà chimico-fisiche e farmacocinetiche di **WSCP1-17** hanno evidenziato che alcuni profarmaci possiedono migliori profili di solubilità in acqua e lipofilia se confrontati con quelli del Carvacrolo tal quale. Studi di stabilità enzimatica, valutata in plasma umano e nei fluidi gastrici ed intestinali simulati in presenza rispettivamente di pepsina (3.2 mg/mL) e pancreatina (10 mg/mL), hanno rivelato che essi risultano molto stabili nei fluidi gastrici rispetto a fluidi intestinali (SIF) e plasma umano. La valutazione dell'attività antimicrobica di **WSCP1-17** è stata eseguita su batteri Gram positivi [*S. aureus* (MSSA, *S. aureus* meticillino-sensibile; MRSA, *S. aureus* meticillino-resistente), *S. epidermidis*, *S. agalactiae*, *S. pneumoniae*, *S. pyogenes*] e su Gram negativi (*E. coli*, *K. Pneumoniae*, *P.*

aeruginosa, and *A. baumanii*). Tra i profarmaci sintetizzati, **WSCP1-3** che hanno mostrato la maggiore solubilità in acqua hanno anche evidenziato un buon profilo microbiologico.

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SEPARATION OF CO_2 AND CH_4 FROM BIOGAS BY FORMING CHEMICALLY PROMOTED CLATHRATE HYDRATES

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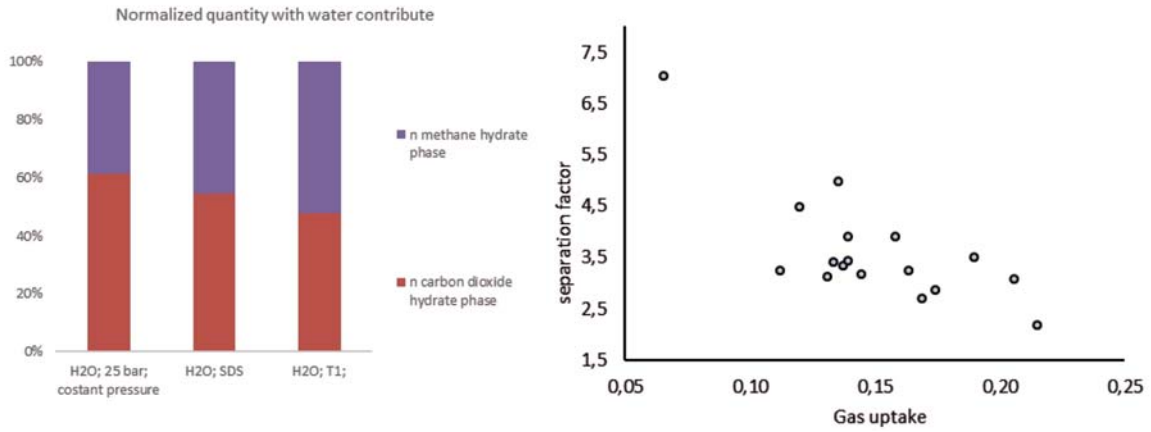
This work reports on the upgrading of model biogas mixtures, typically 60/40 CH_4/CO_2, by chemically promoted clathrate hydrates. Promoters used were several anionic, zwitterionic and cationic surfactants which demonstrated to affect the hydrate-forming ability of water. Some lignin derivatives were also tested as hydrate promoters. Promoted hydrates were also compared to hydrate-based separation starting from non-promoted water. Separation experiments were conducted under pressures of 4 MPa and 2.5 MPa, and temperatures of 1°C and 4°C, both under pressure-dropping and constant pressure conditions. Results show that the separation ability of clathrate hydrates, as determined by the separation factor *S*, is highest when no promoter is added to the water phase; the well known promoter sodium dodecyl sulfate (SDS) shows a value of *S* which is approximately half the value in plain water, while higher separations were obtained with some lignin derivatives and a naphthalene sulfonate derivative.



A) Methane and carbon dioxide into hydrate phase after the separation process as carried out under constant pressure conditions.

B) The picture clearly shows the general behavior where a decrease in the hydrate driving force leads to an increase in the separation factor, S.

We also show that the contribution of CO_2 solubility in water to *S* is a main player in the overall process; also, the separation ability of hydrates seems to be inversely proportional to the amount of gas mixture enclathrated, i.e. the occupancy.

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Produzione e caratterizzazione di network 3D a base di grafene

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Nell'ultimo decennio il grafene, allotropo del carbonio con struttura bidimensionale, è emerso come materiale tra i più promettenti, grazie alle sue straordinarie proprietà chimiche e fisiche che lo rendono estremamente interessante per applicazioni tecnologiche in elettronica, fotonica e più recentemente pure in biomedicina.[1] Le proprietà più sfruttate in campo biomedico sono, sicuramente, l'elevata area superficiale, la flessibilità e l'alta resistenza meccanica. L'ampia area superficiale consente di sfruttare il grafene come "piattaforma" mediante la sua funzionalizzazione covalente e non covalente con molecole di diverse dimensioni; la flessibilità e la resistenza meccanica molto elevate consentono a questo materiale di interfacciarsi con i sistemi biologici.
Tra i diversi derivati, si è deciso di utilizzare il grafene ossido (GO), che seppur non goda delle stesse proprietà del grafene a causa dei difetti superficiali strutturali ed elettronici risultanti dall'ossidazione, ben si presta alla funzionalizzazione con molecole di interesse biologico, data la presenza di differenti gruppi reattivi sulla sua superficie.[2]

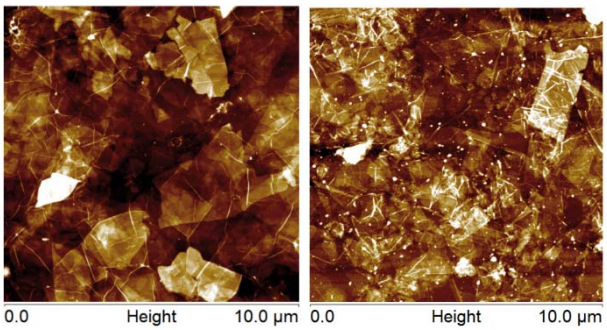

Figura 1 Immagine AFM del grafene ossido (a sx) e del network grafene ossido funzionalizzato con molecole amminate (a dx)

In particolare, nel presente lavoro, il grafene ossido è stato funzionalizzato mediante reazione di apertura di anello dei gruppi epossidi per legare covalentemente alla sua superficie molecole che espongono molteplici gruppi amminici.[3]
L'avvenuta funzionalizzazione che da origine alla formazione del network è stata studiata tramite l'utilizzo di diverse tecniche. In particolare sono state utilizzate la microscopia a forza atomica (AFM) e la spettroscopia fotoelettronica a raggi X (XPS) per ottenere informazioni strutturali/morfologiche e composizionali, rispettivamente.

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Synthesis of Oxazolidinone Derivatives from Propargylic Carbamates

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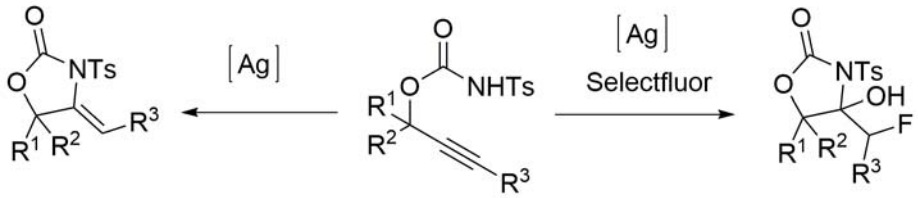
Because of the extensive utility of oxazolidinone derivatives as versatile intermediates in organic synthesis and their use in both the pharmaceutical and agricultural industry, several methods for their preparation are reported in the literature. The most common way of their preparation involves the reaction of an amino alcohol with phosgene or chloroformate as carbonyl precursor.[1] Oxazolidinones can also be synthesized starting from propargylic alcohols, amines, and CO_2 as carbonyl precursor in the presence of metal salts, phosphines, or ionic liquids.[2] Copper-, palladium-, silver- and gold-catalyzed cyclizations of *O*-propargyl carbamates have also been reported.[3]

As part of our continuous research activities aimed to the formation of carbon-heteroatom bond forming reactions, we would like to report the results of our investigations on the unprecedented tandem cyclization/hydroxyfluorination[4] of propargyl carbamates as well as the role of silver catalysis on the cycloisomerization reaction (Scheme 1).



Scheme 1

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THE BIOACTIVE COMPOUNDS OF ABRUZZO'S OFFICINAL PLANTS: EXTRACTION AND CHEMICAL INVESTIGATIONS

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A Bioactive Compound (BC) is a compound which has the capability and the ability to interact with one or more component(s) of the living tissue[1]. The natural occurring BCs can be divided into 5 groups: (a) vitamins and (b) minerals, which represent the nutrient compounds, (c) antioxidants, (d) phytoestrogens and (e) dietary fiber, which represent the non-nutritive compounds. Among the non-nutritive compounds, considerable importance is recovered by the antioxidant substances: any substance that, when present at low concentrations compared to those of an oxidizable substrate, significantly delays or prevents oxidation of that substrate[2]. These substances have different and important biological properties, but they are also of interest in the cosmetic, pharmaceutical and especially in the food industries as biopreservatives.

The natural extracts production and the BCs with antioxidant activity extraction, are usually realized through different methods: (a) conventional, distillation (steam or hydro-distillation – SD/HD), maceration and solid-liquid extraction; (b) unconventional, ultrasound[3], microwave[4], supercritical fluid extraction[5] and accelerated solvent extraction[6]. The unconventional methods were recently developed and they are more environment compatible, thanks to the reduced use of organic solvents, shortened operating times and improved yield and quality of the extracts[7]. Among the innovative extraction techniques, the Rapid Solid-Liquid Extraction Dinamic – RSLDE obtained by Naviglio Extractor®, recovers considerable importance in the natural extracts production[8]. The generation within the system, with an appropriate solvent, of a negative pressure gradient between the outside and the inside of a solid matrix, followed by a rapid restoration of the initial equilibrium conditions, induces the forced extraction of compounds not chemically bonded to the main structure of the matrix[9]. The production of natural extracts, mainly obtained from medicinal plants in recent years, has gained considerable importance in both the scientific and commercial fields.

The natural extracts exhibit biological activity greater than the individual purified compounds, thanks to the presence of positive synergistic effects between the different BCs[10].

In the Abruzzo region's territory, the cultivation of officinal plants contributes significantly to the regional economy. Among the crops cultivated the species *Allium sativum* L., *Cannabis sativa* L., *Coriandrum sativum* L., *Rosmarinus officinalis* L., *Thymus vulgaris* L., showed interesting biological activities in different studies[11,12].

This work has been focused on the extraction of bioactive compounds by means of SD and HD, for the production of essential oils (EOs), and RSLDE, for the production of ethanolic and aqueous extracts. The plant matrices were collected from Abruzzo farmers practicing organic agriculture.

The EOs and the extracts obtained were investigated for their composition: the chemical characterization of the OE was carried out by GC-MS, while the RSLDE extracts were subjected to concentration and clean-up procedures, in order to analyze their chemical composition by the mean of different chromatographic techniques.

The GC-MS chemical characterization of the EOs revealed as main compounds: diallyl trisulfide (45%) and diallyl disulfide (35%) for *A. sativum*; myrcene (49%) for *C. sativa*; linalool (80%) for *C. sativum*, camphor (18%), borneol (16%), 3-carene (13%) and eucalyptol (10%) for *R. officinalis*; thymol (42%) and 3-carene (20%) for *T. vulgaris*.

The antioxidant activity (AOC) and the total phenolic content (TPC) were evaluated in vitro using different spectrophotometric assays: ABTS / TEAC, FRAP, DPPH and Folin-Ciocalteu, respectively. The AOC and TPC assays showed good results for all EOs tested (Fig. 1). Among the extracts the best results were observed for *T. vulgaris* (TEAC / ABTS: 31,2 ± 1,9 µmol Trolox/g dw; Folin-Ciocalteu: 157.5 ± 26.4 mg GAE/g dw).

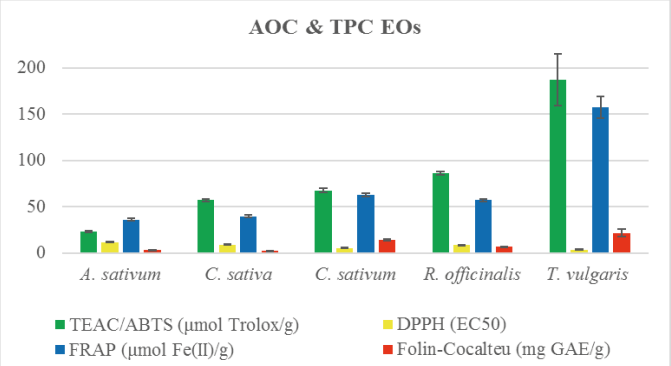

Fig. 1 - AOC and TPC results for the assayed EOs

The results obtained indicate an interesting potential of the tested EOs and extracts for a possible industrial application as food preservatives. This type of evaluation usually takes a few years, in order to assess the impact of climate and soil factors on the synthesis of secondary metabolites, and then on the composition of the natural extracts.

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SPME-GC-MS to analyze volatile organic compounds produced during cooking

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The aim of this study was to set up a new system allowing to analyze volatile organic compounds (VOCs) emitted during cooking by solid-phase microextraction and gas chromatography coupled to mass spectrometry (SPME-GC-MS). Sampling was performed by inflating an olfactometric bag with the VOCs containing air produced during a cooking process. The bag allows to transport the sample to the instrument location and to perform the SPME extraction of the sampled air. The efficiency of different systems to perform the SPME extraction from the air contained in the bag was assessed by using a standard mixture of alkanes from *n*-C5 to *n*-C18 in order to obtain a sufficient sensitivity. The system was then used to extract and analyse VOCs from air produced during frying fries in sunflower oil. Different SPME extraction times were evaluated. Shorter extraction times allowed to extract better certain compounds, like hexane, 2-methyl-1,3-dioxolane, butanol, while longer extraction times allowed to enhance the extent of extraction of other compounds like (*E*,*E*)-2,4-decadienal, 2-undecenal, 2,6-dimethylheptadecane, (*Z*)-8-hexadecene. Thus, the set up system, combining the use of olfactometric bags and the SPME-GC-MS, is applied for the first time to the study VOCs emitted during cooking and it allows to perform the analysis, even on samples produced in sites far from the instrument location, in an easy way and with instrumentations available in most of the laboratories. Preliminary results of the study will be presented and discussed.

Cerium oxide particles functionalized with phosphonic acids for radical scavenging use in PEMFC

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Proton exchange membrane fuel cells are one of the future power sources due to their ability of converting chemical energy into electricity. The biggest issue of this technology is membrane both mechanical and chemical degradation. The first one is due to not uniform contact pressure or to fatigue from stress resulting from humidity cycling; the second one is due to the presence of contaminants, which generate free radical species[1] that damage the membrane provoking the thinning of the membrane. To reduce these phenomena, one possible way is to use radical scavenger species as membrane fillers. Cerium oxide has attracted much attention because of its numerous technological applications. Many of these arise from the facility of Ce^{3+}/ Ce^{4+} redox couple and the high mobility of nonstoichiometry induced oxygen vacancies in nanosized ceria materials[2]. Cerium oxide has been obtained by controlled oxidation of soluble Ce(III) in hydrothermal conditions. In optimal conditions, crystallized nanoparticles with average size of 10 nm and different shape, nanopolyhedrals, nanocubes and nanorods, were obtained. Our aim is to immobilize the CeO_2 particles in the hydrophobic region of the perfluorophosphonic acid membrane (PFSA) by grafting fluorophosphonic acids on the oxide surface promoting the interaction with the perfluorinated PFSA backbone. The chosen acids were 3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10 heptadecafluorodecylphosphonic acid and 2,3,4,5,6-pentafluorobenzylphosphonic acid. The functionalization reactions were carried out by changing temperature and the amount of acid needed to form a monolayer on the particle surface. ICP analysis on phosphorus confirmed the functionalization, showing a reasonable amount of P per g of CeO_2. The efficacy of functionalized nanoparticles in mitigating PEM degradation from free radical will be investigated.

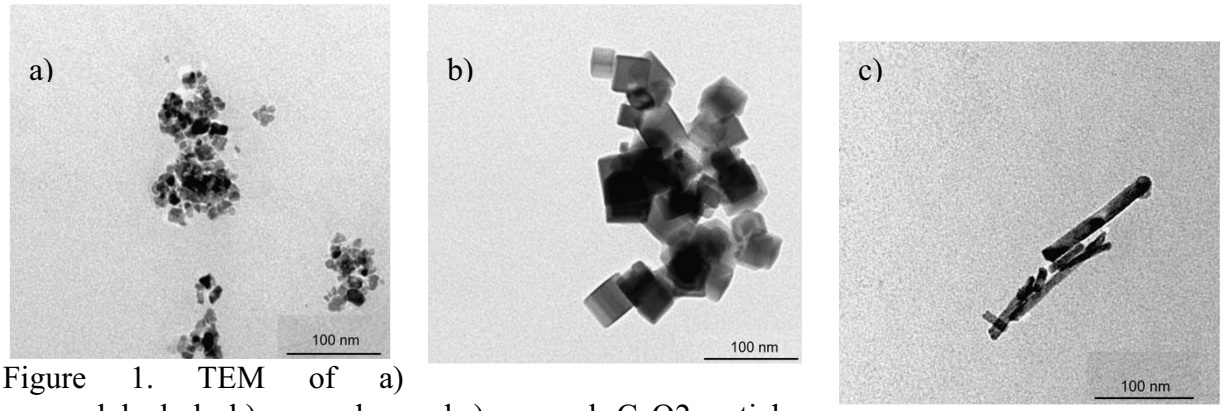

Figure 1. TEM of a) nanopolyhedrals, b) nanocubes and c) nanorods CeO2 particles.

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DESIGN, SYNTHESIS AND BIOLOGICAL EVALUATION OF NEW PYRAZOLOBENZOTHIAZINE ANALOGUES AS p38α MAPK INHIBITORS

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p38 mitogen-activated protein kinases (MAPKs) are serine/threonine protein kinases that play a key role in cellular responses to external stress and regulate the secretion of several inflammatory mediators.[1] Many efforts have been made to develop p38 MAPK inhibitors selective for α and β isoforms, potentially useful for the treatment of chronic inflammatory and autoimmune diseases.[2] More recently, interest has turned towards other indications such as chronic obstructive pulmonary disease, pain, cardiovascular and neural diseases, and cancer.[3] However, inhibitors have failed in the clinical trials either due to poor pharmacokinetic profile or selectivity issues. For these reasons, p38 MAPKs drug discovery represents an intriguing research field.

Recently, we reported on the identification of a pyrazolobenzothiazine-based chemotype as p38α MAPK inhibitors worthy of future chemical optimization. [4]

Within this first series, compound **1** was the best hit showing sub-μM inhibitory activity against in-vitro p38α screening as well as TNF-α release assays coupled with a promising kinase selectivity profile.[4]

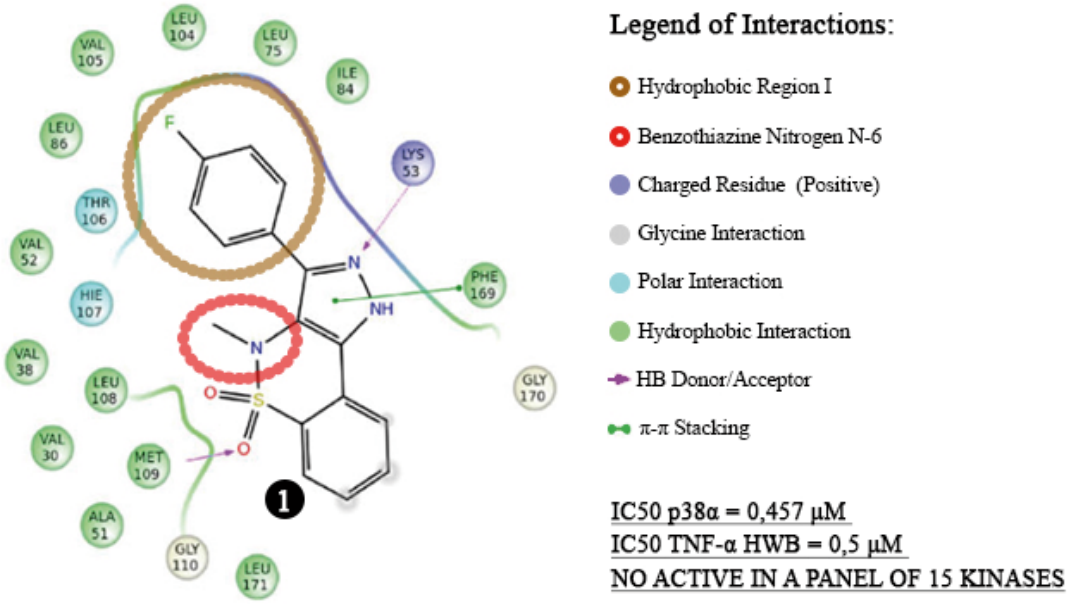

Figure 1: Legend of the interactions between the hit compound **1** and the receptor pocket.

Starting from the hit compound **1** as template the optimization strategy entailed:

- The design of close analogues, characterized by the same pyrazolobenzothiazine core with the most of changes focused on the hydrophobic region 1 (HR1) and on the benzothiazine nitrogen (6N). In particular the HR1 was functionalized with different halogens, a methyl and combining these two chemical moieties. Furthermore the N-6 position was alkylated with different aliphatic chains.
- The arrangement of two isosteric replacements with a dibenzothiazine and an isoxazolobenzothiazine, respectively.
- A docking study as support and validation of the entire design process.

Herein we report a rigorous approach entailing the design, synthesis and biological evaluation of a new series of promising p38 MAPKs inhibitors.

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PEPTIDI INIBITORI DEL QUORUM SENSING INCAPSULATI IN NANOPARTICELLE POLIMERICHE PER L'ERADICAZIONE DEL BIOFILM DA *S. AUREUS*

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Si stima che oltre il 60% delle infezioni batteriche nell'uomo presentano la formazione di biofilm microbici[1]. In particolare, *S. aureus* è riemerso come agente patogeno, clinicamente rilevante, per la sua presenza nell'ospite umano sotto forma di biofilm.

La caratteristica matrice polimerica extracellulare di quest'ultimo presenta diversi vantaggi per i batteri, tra i quali la capacità di eludere i meccanismi di difesa dell'ospite e una spiccata tolleranza agli antibiotici[2].

Uno degli approcci recenti per la riduzione della virulenza causata da *S. aureus* in forma di biofilm è rappresentata dalla riduzione della comunicazione cellulare batterica, nota come *Quorum Sensing* (QS), che è di fondamentale importanza per l'organizzazione del biofilm stesso[3]. Nel caso di *S. aureus* il QS è mediato dall'*RNA-III-activating peptide* (RAP) e il suo recettore TRAP.

L'eptapeptide *RNA III-inhibiting peptide* (RIP) è in grado di contrastare efficacemente il QS batterico, inibendo la fosforilazione del recettore TRAP, con conseguente ridotta adesione del biofilm su superfici e l'inibizione della sintesi di tossine e proteine di adesione[4].

Nel 2013 Baldassarre *et al.*[5] sintetizzarono una serie di peptidi strutturalmente correlati al RIP per valutare il contributo di ciascun amminoacido sull'attività antimicrobica. Uno degli analoghi, FS10, ha espresso la maggiore attività tra i composti sintetizzati, rappresentando quindi un buon candidato per lo sviluppo di un nuovo *tool* terapeutico in grado di contrastare la formazione del biofilm da parte di *S. aureus*. In alcuni casi la somministrazione di peptidi come entità terapeutiche non è semplice da realizzare, a causa di una serie di difficoltà: suscettibilità alla degradazione gastrointestinale, rapida eliminazione in vivo, breve emivita in fluidi corporei, scarsa permeazione attraverso le membrane fisiologiche e instabilità durante la conservazione a temperatura ambiente. L'incorporazione di proteine in nanoparticelle polimeriche di acido poli(lattico-co-glicolico) (PLGA) fornisce protezione contro idrolisi *in vivo* e mantiene la loro attività inalterata, incrementando potenzialmente la biodisponibilità[6]. Tuttavia, l'inclusione di proteine in nanoparticelle polimeriche spesso presenta alcune sfide e problematiche di tipo formulativo. L'elevata idrofilia di RIP e FS10, unita al loro basso peso molecolare, causa deboli interazioni con le catene polimeriche rendendo l'incapsulamento difficile da ottenere.

Lo scopo di questo progetto è migliorare l'intrappolamento di RIP e FS10 in nanoparticelle di PLGA come alternativa per superare tutti i problemi precedentemente riportati, considerando vari parametri formulativi al fine di migliorare l'accumulo dei peptidi in *carriers* polimerici, compresi vari metodi di preparazione, l'influenza del pH della fase acquosa esterna e l'effetto di diverse miscele polimeriche.

In particolare, le ultime due strategie, combinate insieme, hanno permesso di migliorare l'efficienza di incapsulamento dall'1.8% al 22% per FS10 e dal 20% fin oltre il 50% per RIP, rispettivamente. E' stato teorizzato che un pH elevato riduce la carica dei peptidi, diminuendo di conseguenza la loro migrazione nella fase acquosa, e incrementando quindi la quantità di peptide all'interno delle nanoparticelle. Ulteriori dati riguardo stabilità e profili di rilascio saranno trattati durante la comunicazione orale.

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Study of the catalytic activity of *cis*-dioxomolybdenum(VI) catalysts bearing α-aminoacid ligands, for mild and selective oxyfunctionalization of olefins

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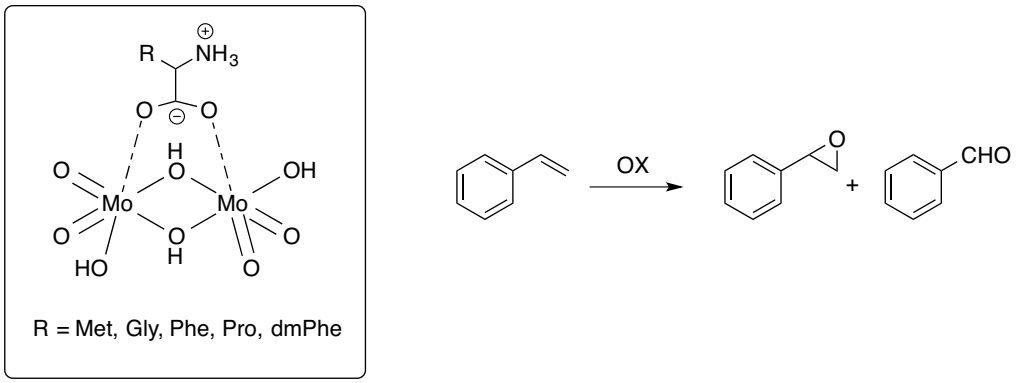
Molybdenum forms part of the active sites of metalloenzymes that execute key transformations in the metabolism of nitrogen, sulfur and carbon compounds.[1] It is of essential importance for (nearly) all biological systems and the enzymatic role of its compounds in biological reactions has created a tremendous impetus in the synthesis of a number of model complexes mimicking oxotransferase molybdoenzymes for their application in the catalytic metal-based oxygen atom transfer (OAT) reactions.[2]



Figure

In this regard, many stable molybdenum complexes with oxygen-, nitrogen- and sulfur-containing ligands have been prepared. Possessing a *cis*-MoO_2 core unit, they have frequently been used as catalysts in industrial processes, such as epoxidation, sulfoxidation and hydroxylation of olefins.

In this communication, the results we have recently obtained in the study and optimization of the catalytic activity showed by a series of Mo(VI) complexes of general formula $[Mo_2O_4(OH)_4(aaH)]$,[3] where *cis*-MoO_2 units are linked by a zwitterionic aminoacid ligand, *via* a bidentate bridging coordination through the carboxylate group (Figure), in the selective oxyfunctionalization of conjugated and unconjugated olefins by means of activation of *tert*-butyl hydroperoxide, are presented.

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Liposomi funzionalizzati con mannosio-6-fosfato come Targeted Delivery Systems (TDS)

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Lo sviluppo di nuovi carriers per il delivery di farmaci rappresenta una fase importante per l'ottenimento di nuovi sistemi terapeutici efficienti e selettivi. In particolare in campo oncologico le nanotecnologie consentono potenzialmente di superare molti problemi legati all'impiego della maggior parte dei farmaci chemioterapici i cui effetti collaterali sono spesso molto aggressivi e invalidanti. In questo studio proponiamo la sintesi di nanoparticelle lisosomotropiche basate su liposomi contenenti colesterolo funzionalizzato con mannosio-6-fosfato (Fig.1). Grazie alla sua affinità per il CI-M6PR (recettore del mannosio-6-fosfato catione indipendente), il gruppo M6P consente ai liposomi di trasportare molecole bioattive lungo il percorso che porta ai lisosomi permettendo a tutto il sistema supramolecolare di penetrare nella cellula con il carico di farmaco. Allo scopo di ottenere un sistema di targeted drug delivery riconosciuto dal recettore CI-M6PR abbiamo sintetizzato un derivato del colesterolo (Chol-M6P) in cui un mannosio 6-fosfato è legato covalentemente al colesterolo.

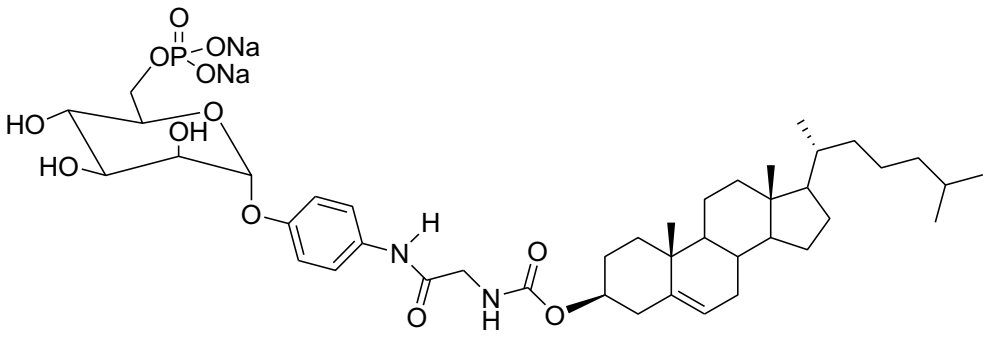

Figura 1

Tale lipide è stato impiegato con la dipalmitoilfosfatidilcolina nella preparazione di liposomi oligolamellari che sono stati caratterizzati mediante Dynamic Light Scattering e Electrophoretic Light Scattering allo scopo di determinarne le dimensioni ed il potenziale zeta. E'stata inoltre valutata la stabilità delle nanoparticelle nel siero (FBS, fetal bovine serum) mediante turbidimetria e DLS. Lo scopo della nostra ricerca è infatti quello di sfruttare un targeting attivo per il rilascio di farmaci anti-cancro nelle cellule tumorali attraverso il CI-M6PR, il quale è abbondantemente espresso in diversi tumori umani, in particolare nelle fasi precoci del cancro al seno[1]. Studi recenti[2] inoltre, hanno evidenziato una maggiore espressione del recettore del mannosio-6-fosfato nelle cellule di adenocarcinoma mammario,

le MCF7, rispetto ad altre linee di cellule tumorali ma soprattutto rispetto a cellule primarie non tumorali fra cui i fibroblasti.

Per mezzo di analisi di microscopia a fluorescenza e microscopia confocale abbiamo innanzitutto dimostrato la capacità dei liposomi funzionalizzati di essere internalizzati da cellule che esprimono il CI-M6PR. In particolare è stata dimostrata la capacità del nanocarrier di raggiungere i lisosomi e di rilasciare nel lume lisosomiale le molecole trasportate. Questo risultato indica che tali nanoparticelle sono in grado di mediare un riconoscimento specifico del recettore del mannosio-6-fosfato. Abbiamo quindi valutato l'internalizzazione intracellulare dei liposomi funzionalizzati nelle cellule MCF7 mediante analisi citofluorimetrica. Per valutare infine l'applicabilità dei liposomi funzionalizzati come Targeted Drug Delivery System abbiamo dimostrato la citotossicità selettiva dei nostri sistemi nei confronti di cellule tumorali MCF7 utilizzando come controllo non tumorale cellule primarie di fibroblasti umani, le HDF. Trattandosi di un sistema di rilascio lisosomotropico è possibile indurre citotossicità nella cellula bersaglio utilizzando farmaci in grado di indurre il fenomeno LMP (Lysosome Membrane Permeabilitation) come la Ceramide-C6, un precursore della sfingosina. Infatti è stato dimostrato che l'accumulo di Ceramide-C6 all'interno dei lisosomi provoca la permeabilizzazione della membrana lisosomiale in modo simile a come fanno i detergenti, con conseguente rilascio degli enzimi lisosomiale e apoptosi[3].

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Analisi fluidodinamica di digestori anaerobici

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La digestione anaerobica è la tecnologia più diffusa per il trattamento della biomassa per la produzione di biogas. Il mixing è il più importante parametro per avere una digestione anaerobica altamente efficiente[1]. In tale contesto, la fluidodinamica computazionale può fornire una modellizzazione dell'idrodinamica e del mixing all'interno dei sistemi di digestione anaerobica[2]. In questo lavoro un'analisi computazionale è sviluppata per stabilire la migliore configurazione geometrica e il sistema di mescolamento tra differenti digestori anaerobici, valutando i profili di velocità e temperatura. Il software COMSOL Multiphysics™ 4.2 è utilizzato a tale scopo. Due differenti scenari avente uno l'ingresso del fluido in direzione laterale e l'altro sulla sommità sono considerati; il sistema di mescolamento è ottenuto tramite delle pompe esterne per il ricircolo del fango. Caratteristiche del liquame sono: densità, viscosità, solidi totali rispettivamente pari a 1001.73 kg/m^3, 2 Pa·s e 12 %w/w. La temperatura all'interno del digestore è compresa tra 308-318 K e poiché avviene una reazione biologica endotermica viene fornito del calore dall'esterno tramite uno scambiatore posto su una parete esterna. Le equazioni di continuità, momento e turbolenza (turbolenza standard k-ε, basso numero di Reynold) sono fissate per ottenere i profili di velocità risolvendo il modello Euleriano e assumendo per la fase liquida una legge di potenza non-Newtoniana[3]. Equazioni di conduzione e convenzione sono utilizzate per tracciare profili di temperatura. In prossimità della parete viene fornita una potenza pari a 25.8 kW, mentre all'interno si liberano 12 kW di calore endotermici. Flussi di campo, media, varianza, deviazione standard della velocità media e gradienti di velocità sono i parametri analizzati, in aggiunta ai profili di temperatura del liquame. I risultati delle simulazioni suggeriscono che la configurazione nella quale il fluido entra in direzione tangente alla superficie (figura 2) è la migliore soluzione poiché consente di avere una maggiore omogeneità del sistema di mescolamento. Media, varianza, deviazione standard della velocità media e gradiente di velocità sono rispettivamente uguali a 0.01522 m/s, 0.00006 m/s, 0.00758 m/s, 75 1/s. Inoltre a parità di potenza termica fornita e sottratta si raggiunge una maggiore temperatura, pari a 314 K. La fluidodinamica computazione è quindi una promettente tecnologia per analizzare il mixing all'interno di digestori anaerobici. La futura costruzione del digestore anaerobico consentirà di verificare i risultati ottenuti.

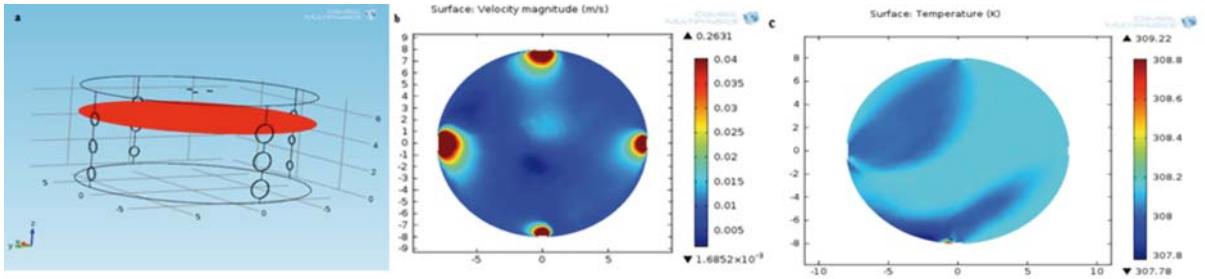

Figura 1 Risultati delle simulazioni per il digestore anaerobico (soluzione A): a-piano all'interno del digestore anaerobico di equazione z=5 m; b-profili di velocità per il piano di equazione z=5 m; c-profili di temperatura per il piano di equazione z=5 m.

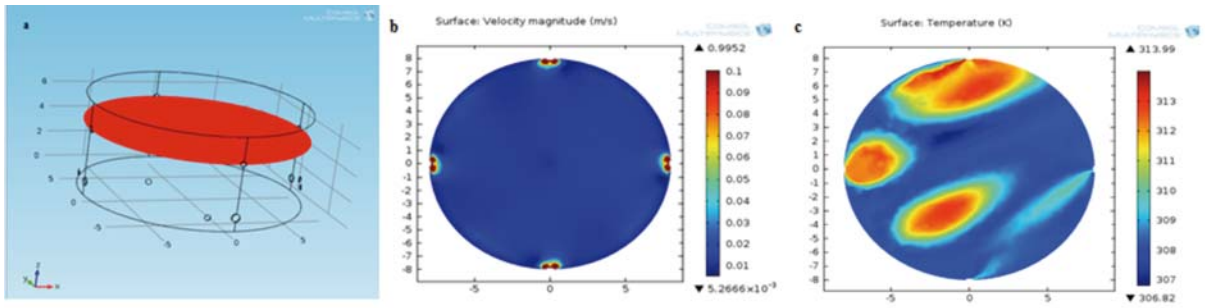

Figura 2 Risultati delle simulazioni per il digestore anaerobico (soluzione B): a-piano all'interno del digestore anaerobico di equazione z=5 m; b-profili di velocità per il piano di equazione z=5 m; c-profili di temperatura per il piano di equazione z=5 m.

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Fragment-Based Drug Discovery Applied to Trypanosoma Brucei PTR1. Discovery of Two Lead Series with High Ligand Efficiency

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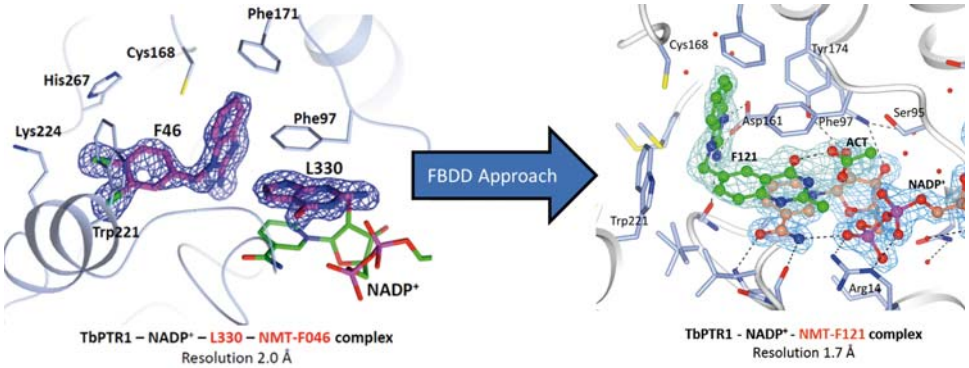
According to World Health Organization (WHO), parasitic diseases, such as African (sleeping sickness) and American (Chagas disease) trypanosomiasis and Leishmaniasis, afflict over three billion people in the world. Drugs currently in use have major limitations due to their significant toxicity, variable efficacy, low bioavailability and development of resistance. There is a clear necessity to discover new targets and new drugs to treat these diseases.
Trypanosomatids lack the ability to synthesize folates de novo and are totally dependent on the salvage of extracellular folates for growth. However, antifolates cannot be used in therapy of trypanosomatidic infections because dihydrofolate reductase (DHFR) inhibition is compensated by another enzyme, the pteridine reductase-1 (PTR1). PTR1 is mainly involved in the reduction of biopterine but can also reduce folates, thereby safeguarding the cell survival. Therefore, PTR1 could be a promising target for the design and the development of new antiparasitic drugs. [1] To address these issues, we started a fragment-based drug design (FBDD) approach to improve the quality and (most importantly) the efficiency of the drug discovery process.



The X-ray crystallography screening identified several pteridin-like fragments with affinity ranging between 10^{-3}-10^{-4} M Ki values. A subsequent structure-based design, guided by previously published structural data, allowed their optimization into two series of compounds with high affinity and good ligand efficiency. Structure–activity relationships were

established, and more potent molecules were designed and synthesized using fragment growth and fragment linking strategies. All the synthesized compounds were evaluated for their capability to inhibit parasitic PTR1 as well as other parasitic folate-dependent enzymes (TS and DHFR) in an enzymatic assay. The early tox profile has been also determined. All the assays have been performed through HTS technologies. Seven new crystallographic structures of the developed compounds were also obtained in a ternary complex with TbPTR1-NADPH and the poses support the design reproducing the poses and retaining the key interactions of the initial binding fragments, additionally exploring other areas of the PTR1 binding site. All the compounds have been tested against the different parasites as single agents and in combination with methotrexate revealing a good antiparasitic activity, selectivity and synergy against T. brucei. The progress of the compounds in the pipeline was strengthening with the concept of Target Profile concept (TPP) to reduce the liabilities of the drug candidates allowing us to identify the best candidates for further in vivo studies, such us the determination of the SNAP-PK and antiparasitic activity on mice.
The results obtained are in line with the FBDD approach allowing to achieve, with swift and aimed scaffold improvement, a sustainable delivery of high-quality lead candidates.
This work was supported by NMTrypI (New medicine for Trypanosomatidic Infections) and received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no.603240. www.nmtrypi.eu

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Difunctional folic acid-octapeptide bioconjugate engineering to intracellular trafficking anticancer target

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The human Thymidylate synthase (hTS) plays a crucial role in the early stages of DNA biosynthesis, representing a very important "house-keeping" protein enzyme for the cellular-growth and -survival. It catalyzes the methylation reaction of 2'-deoxyuridine monophosphate (dUMP) to provide the only cellular source of 2'-deoxythymidine monophosphate (dTMP), by using a folate moiety as cofactor substrate. For this reason, hTS has become an important target for anticancer treatment(1). In our efforts to discover new anticancer agents specifically directed to hTS, we identified some new peptide-based inhibitors designed from the monomer-monomer interface of hTS. Among these, the peptide LR (***L***SCQLYQ***R***) and some of its derivatives have been shown able to inhibit hTS enzyme activity acting on a previously unknown binding site with a new dual-mechanism of action, as shown by X-ray crystal structure of the LR-peptide/hTS complex. They are able to block the protein catalytic function by stabilizing its inactive structural form and, on the other side, to inhibit the cell growth of cisplatin (cDDP)-sensitive and -resistant human ovarian cancer cells (OC), without causing enzyme overexpression(2). Based on the structural analogy between folic acid (FA) and folate cofactor substrate used by the enzyme(3), we speculated the possibility to improve the inhibition efficacy of the peptide against hTS by combining the two fragments, FA and the LR-peptide, in order to attempt a targeted delivery approach by exploiting folic receptor α (FRα)-mediated intracellular trafficking of the FA-LR bioconjugate. In this way, the FRα targeting strategy is expected to afford higher selectivity towards cancer cells overexpressing FRα, such as ovarian cancer cells. In order to identify the most responsive potential targets for a FR-mediated directed therapy, we selected and characterized eight OC cell models, based on FR expression levels, by exploiting both quantitative and semi-quantitative methods, including flow cytometry, Western Immunoblotting, real time PCR and radio-ligand binding assays. Among these, the IGROV-1 and OAW28 cell lines resulted to express the higher levels of surface receptor protein. Our substrate specificity competitive studies with [^{3}H]-folic acid demonstrated that FA-LR targets OC cells via FRα with an affinity comparable with that of FA and in a manner dependent by the FRα expression levels rate, as also confirmed by the performed molecular modeling simulations(4). We have extensively studied the inhibition pattern of recombinant hTS by the LR-peptide and its bioconjugate with FA. The first formally exhibits a competitive inhibition with an apparent Ki value equal to 90±7μM, while the behavior of FA-peptide conjugate is better accounted for in terms of non-competitive inhibition, with an apparent Ki value of 40±15μM. These data are in according with the difunctional nature and dual binding mode of

FA-LR conjugate. These experimental data were also supported by the performed docking simulations studies, highlighting a binding preference for FA-LR conjugate to the monomer-monomer interface of the hTS enzyme but also the possibility for binding to the active site of the protein. We have also developed a label-free spectrofluorometric assay to quantify the internalized FA-LR conjugate into cancer cells, exploiting the fluorescence emission of the pteroate moiety of FA, estimating a three-fold increase of FA-LR in IGROV-1 cells relative to the external incubation concentration(5). The concentration estimates obtained in this way were suddenly confirmed by a high-sensitivity LC-MS/MS approach. The bioconjugate was found to be internalized via both the FRα-mediated and FRα-independent mechanisms and, reached intracellular concentrations of several micromoles/liter, at which the FA-peptide bioconjugate showed a cell-growth inhibitory activity comparable with that of 5-FU, a traditional hTS inhibitor. In conclusion, we have developed a bioconjugate compound, FA-LR, made by a hTS lead candidate inhibitor (LR peptide) and FA. It can specifically interact and bind the FRα in OC cells and be thus internalized. The presented strategy approach may allow to avoid the toxicity effect, as FRα results undetected in normal cells. In this way, the developed folate-peptide conjugate could show the potential to be developed into a new tool for cancer chemotherapy. Our future efforts will focus on lead optimization, cellular pharmacokinetic properties and the biological effects of the new conjugates in cancer cells.

Acknowledgement

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Ritenzione di configurazione nella sintesi, via microonde, di bioisosteri 1H-tetrazolici chirali da derivati fenil propionici.

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Il dolore cronico rappresenta un considerevole problema sociale ed economico.
Evidenze suggeriscono che C5a, proteina prodotta dall'attivazione del complemento, abbia una potente attività nocicettiva quando interagisce con il suo recettore C5aR. [1, 2]
Nel programma discovery della Dompé è stata identificata una classe di acidi (R)-4-(eteroaril) fenil propionici, di cui l'hit compound è la molecola DF2703Y (1a, Fig.1), che ha mostrato una buona selettività e potenza di inibizione della chemiotassi indotta dal C5aR.

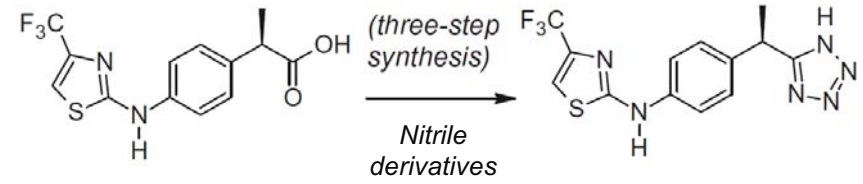

Figura 1

Il programma di lead optimization ha consentito lo studio di una cospicua serie di bioisosteri dell'acido carbossilico,[3] identificando nel tetrazolo il miglior gruppo funzionale e nel DF3966Y (4a, Fig. 1) il lead compound, per migliore profilo farmacologico (ADME e PK), potenza e selettività.
Dal punto di vista sintetico, il punto chiave è il passaggio attraverso l'intermedio nitrile e la successiva reazione con trimetil stannil azide che è risultata essere la via più conveniente per preservare il centro chirale dalla racemizzazione.
La procedura, che è stata applicata a numerosi feniletil-nitrili chirali nonché a derivati della fenilglicina N-protetta, consente di creare analoghi tetrazolici preservandone la chiralità.[4]

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Gold(I) and Gold(III) catalyzed cycloaddition/cyclization reactions of vinylindoles with allenes

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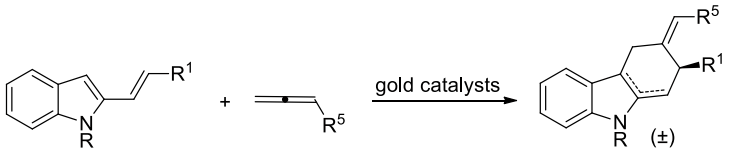
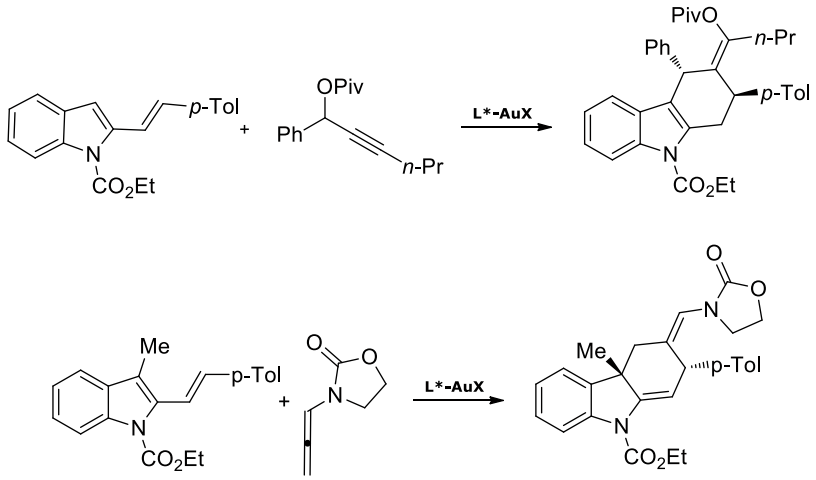
In the last year we developed several strategies to access carbazole derivatives through [4+2] cycloaddition reactions of 2-vinylindoles with allenes under gold catalysis. Application of cationic gold(I) and gold(III) catalysts as π-activators allowed for the chemo-, regio- and diastereoselective construction of complex and intriguing architectures, Scheme 1.[1,2]



Scheme 1

More recently we are focusing on the enantioselective version of these and related reactions. In particular, we are currently studying the enantioselective version of our cascade reaction between 2-vinylindoles and propargyl esters and between a new class of 2-vinylindoles bearing a methyl group at C-3 position with allenamides for the synthesis, respectively, of enantioenriched tetrahydrocarbazoles and dearomatized indole derivatives, Scheme 2.



Scheme 2

A complete survey of catalyst/ligand screening as well as scope and proposed reaction mechanisms will be reported.

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Efficient Synthetic Methodologies to Extend the Corrole Ring Conjugation

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In the last decade the structural elaboration of corrole macrocycle at both *meso*-aryl and/or *β*-pyrrolic positions has experienced notable advancements, enabling the preparation of a wide range of *meso*-triarylcorroles with tunable properties. The variety of the achievable corrole derivatives has allowed a more deepened knowledge of the properties of these macrocycles, prompting their practical use in many applications, ranging form catalysis to dye-sensitized solar cells[1]. The mandatory step to modify the corrole periphery is the development of efficient synthetic methodologies to introduce valuable functionalities as formyl, nitro or halo groups, which are easily modifiable by further organic reactions. Among the uncountable synthetic manipulations, we are interested in exploring the extension of the corrole π-system, since this modification can significantly enhance the photophysical properties of the macrocycle. With this goal in mind, we developed two different approaches, that are illustrated in Figure 1, for the insertion alkynyl groups[2] and the fusion of pyrazino or pyrrolopyrazino units [3,4] on the corrole β-pyrrolic positions. In the first case, a regioselective bromination protocol was developed to give a dibromosubstitued macrocycle, subsequently used in the Stille cross coupling reactions. In the latter case, a nitro- amino- corrole derivative was the key compound subjected to a series of organic reactions which leads to the β-annulation. The developed synthetic strategies and the results obtained will be showed and discussed in details during the presentation.

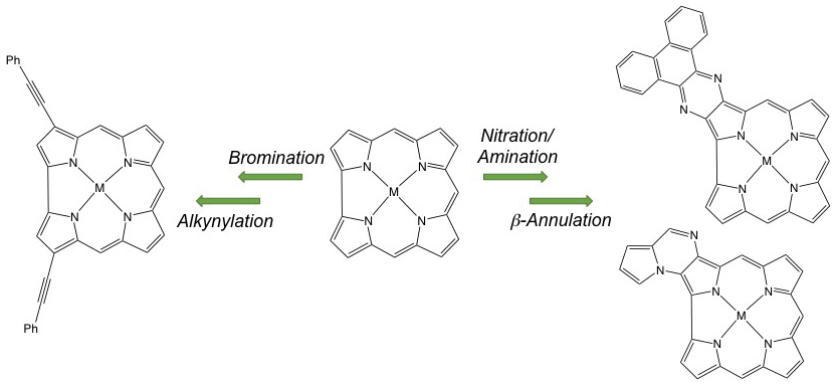

Figure 1

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LEGAME CON IL TERRITORIO DI ORIGINE DI CACIOCAVALLI MOLISANI: STUDIO TRAMITE APPROCCIO "UNTARGETED" IN SPETTROSCOPIA ^{1}H-HR-NMR

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Gli approcci "untargeted" basati sullo studio delle "impronte digitali degli alimenti" (food fingerprinting) sono considerati sempre più potenti mezzi di indagine in processi di autenticazione aventi per scopo la caratterizzazione globale di matrici alimentari complesse. Le matrici alimentari possono essere indagate riguardo l'origine geografica, le varietà di specie, le possibili adulterazioni, ecc. per mezzo di analisi chimiche spettroscopiche o spettrometriche "untargeted" seguite da una valutazione statistica multivariata dei dati acquisiti.[1] Nelle matrici alimentari la tipologia e la quantità di metaboliti presenti derivano dalla combinazione di numerosi fattori concomitanti legati ad esempio alla zona di produzione, alle materie prime impiegate per l'ottenimento del prodotto, alle tecniche produttive utilizzate, all'alimentazione degli animali, alla stagionalità ecc. Tale combinazione di fattori potrebbe risultare caratterizzante del prodotto stesso al punto di fornire una sorta di "impronta digitale" dell'alimento. Il profilo dei metaboliti presenti nell'alimento può essere ottenuto tramite la spettroscopia di Risonanza Magnetica Nucleare ad alta risoluzione (HR-NMR), tecnica che sta riscuotendo crescente consenso nella ricerca in ambito alimentare.[2,3]

Verranno illustrati strategie analitiche e risultati di uno studio dove l'approccio "untargeted" e l'analisi statistica multivariata sono stati applicati a 101 spettri ^{1}H-HR-NMR relativi a campioni di Caciocavallo estratti in acqua deuterata. Dei 101 campioni, 50 sono stati prelevati da due aziende molisane e 51, prodotti in diverse regioni italiane, sono stati acquistati sul mercato. Lo studio ha permesso di costruire modelli preliminari di classificazione e predizione in grado di discriminare i caciocavalli molisani da quelli di altre regioni italiane con buone performance.

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GEOGRAPHICAL CLASSIFICATION OF SAFFRON (*Crocus sativus* L.) BY LINEAR DISCRIMINANT ANALYSIS APPLIED TO THE UV-VISIBLE SPECTRA OF AQUEOUS EXTRACTS

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UV-visible spectroscopy (Figure 1) is conventionally adopted for quality grading of saffron according to the ISO Normative 3632.[1] In particular, assignment of saffron to one of the three quality categories (I, II and III) is accomplished by taking the absorbance values at 440, 257 and 330 nm of aqueous extracts, historically associated with coloring strength, flavor or bitterness strength and aroma strength, respectively. To the best of our knowledge, potentiality of UV-vis spectroscopy for geographical discrimination of saffron has never investigated before. With this purpose, we have applied chemometrics to the UV-vis spectra of saffron spices produced in four different sites of Italy: Sardinia (SA), L'Aquila (AQ), Cascia (CA) and Città della Pieve (CP). In addition, a number of saffron samples were bought in various supermarkets and analyzed. Exploratory principal component analysis applied to the UV-vis spectra of saffron aqueous extracts revealed a clear differentiation of the samples belonging to different quality categories, but a poor separation according to the geographical origin of the spices. On the other hand, linear discriminant analysis based on 8 selected absorbance values, concentrated near 279, 305 and 328 nm, allowed a good distinction of the spices coming from different sites. Under severe validation conditions (30 % and 50% of saffron samples in the evaluation set), correct predictions were 85 and 83%, respectively.

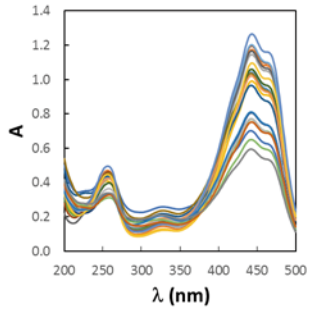

Figure 1

Although the spectrum of saffron aqueous extracts is a complex combination of contributions due to many constituents, the regions useful for geographical identification seems to describe differences in the safranal content, in the flavonoid profile and the proportion of *cis*- and *trans*-crocins. A recent characterization of Italian saffron by HPLC[2] supports the ability of the above substances as geographical markers.

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IL-MAE, UAE ED ESTRAZIONE CONVENZIONALE DI COMPOSTI BIOATTIVI IN RADICI DI *PUERARIA LOBATA* E VALUTAZIONE DELLA LORO ATTIVITÀ INIBITORIA SU ISOFORME DI ANIDRASI CARBONICA

Marcello Locatelli,[a] Simone Carradori,[a] Adriano Mollica,[a] Simona Riga,[a] Rosita Primavera,[a] Martina Di Francesco,[b] Luigi Menghini,[a] Andrea Angeli[c], Luisa Di Marzio,[a] Daniela Secci,[d] Christian Celia,[a] Claudiu T. Supuran,[c,e].

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Questo lavoro si è proposto l'obiettivo di sviluppare e ottimizzare un metodo analitico per l'estrazione, la separazione e l'analisi quantitativa di isoflavoni (puerarina, genisteina, daidzeina e daidzina) nelle radici di *Pueraria lobata* (Kudzu). L'esigenza di titolare tali analiti nasce dalla possibilità di sfruttarne le proprietà nutraceutiche e fitoterapiche.

Figura 1

I metodi esplorati sono: estrazione con microonde, estrazione con ultrasuoni, estrazione classica. Ciascuno di essi è stato ottimizzato in termini di solvente e tempo di estrazione, aggiunta di liquidi ionici (1-butil-3-metilimidazolio bromuro, IL) e ottimizzazione della loro percentuale. Ottimizzare le estrazioni impiegando non solo una soluzione acquosa al 10% di liquido ionico, ma anche una soluzione alcolica al 10% dello stesso, si è rivelata una buona strategia in quanto è evidente l'omogeneità e la linearità dei dati ottenuti nella "serie" dei corrispondenti estratti e, parallelamente, i valori di concentrazione maggiori per gli estratti con IL rispetto ai corrispondenti estratti ottenuti usando solo etanolo 65°. Secondo obiettivo è stato valutare l'attività inibitoria sulle isoforme 1, 2, 9 e 12 dell'Anidrasi Carbonica umana, in modo da valutarne il possibile eventuale impiego nelle patologie coinvolte. Soprattutto l'inibizione delle isoforme 9 e 12, coinvolte in processi tumorali, potrebbe costituire un ottimo punto di partenza per lo sviluppo di nuove entità terapeutiche con attività inibitoria specifica.[1]

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ELECTROSPRAY IONIZATION MASS SPECTROMETRY: A FASCINATING TOOL FOR EXPLORING THE STRUCTURE OF POLY(IONIC LIQUID)S

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In the past two decades mass spectrometry (MS) has gained increasing attention as a powerful analytical technique in the field of polymer chemistry, especially for the structural elucidation of bio- and synthetic polymers. Since the advent of the soft-ionization techniques, such as electrospray ionization (ESI) and matrix assisted laser desorption/ionization (MALDI), many advances have been made in the development of the MS techniques and in the typology of polymers that can be investigated by them.[1] Poly(ionic liquid)s are a class of polyelectrolytes bearing the well-known ionic liquids (ILs) as monomeric repeating units along the polymer chain. These macromolecules combine the properties of ILs and common polyelectrolytes, attracting growing interest in the fields of chemistry, physics and material sciences.[2] They show rather broad glass transition temperature (T_g) ranges, solubility that varies from polar to less polar organic solvents and high structural variety.[3] Currently, the characterization of PILs is mainly based on nuclear magnetic resonance (NMR) spectroscopy and size exclusion chromatography (SEC). However, the accurate structural determination of these polymers *via* mass spectrometry is considered a remarkable challenge.[4] Herein we report, for the first time, the use of the high-resolution ESI-Orbitrap MS, and ESI-QToF MS for the in-depth structural investigation of a wide variety of halide-containing PILs.[5] The styrenic and acrylate-based polymers, synthesized *via* RAFT polymerization and free radical polymerization techniques, have different imidazolium-, triazolium-, pyridinium-, phosphonium and ammonium-based core structures. In addition, the first MS analysis of poly(ionic liquid)s containing weakly coordinating anions introduced by a fast, simple and quantitative postmodification method is reported.[6] The novel ESI MS protocol has proved to give deep insight into the field of PILs chemistry, and allows further advances in the area of polymer studies by MS.

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Press-Transferred carbon black nanoparticles: a new exclusive transducer for electrochemical sensing

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For the first time the press-transfer (PT) technique[1] was used with the nanostructured carbon black (CB), that acts as exclusive electrochemical transducer. The production of a stable CB nano-dispersion does not require sophisticated procedures; due to this reason combined with the low cost of the material, in recent years the use of CB as a nanomaterial has found an increasing application in electrochemical sensing. CB nanoparticles (CBNPs) electrochemical performances have been correlated to its nano dimension[2]. To exploit the nanomaterials property, CBNPs dispersion was filtered through a PTFE membrane and press-transferred on polymethyl methacrylate (PMMA) substrates (figure 1). Using the transducer fabrication optimized parameters, the CBNPs transferred to PT forms a stable and uniform film. The transducers were characterized by cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), transmission electronic microscopy (TEM), field-emission scanning electron microscopy (FESEM) and current-sensing atomic force microscopy (CS-AFM). The amount of press-transferred CBNPs is the key parameter to obtain films with improved conductivity, which is in good agreement with the electrochemical response. CBNPs films were effectively imprinted, with neither evident micro-cracks nor micro-holes, retaining their good conductivity at the macroscale and meeting successfully the microscale scene, showing unique characteristics.

The analytical performance of the CBNPs transducers was deeply evaluated both off-microfluidic chip and on-microfluidic chip, toward three classes of molecules: neurotransmitters, environmental organic contaminants and food polyphenols. In all the cases, CBNPs film exclusively supported the electrochemical analytes detection with excellent performance. These results revealed the analytical potential of this carbon nanomaterial in the electrochemical field, as well as the suitability and versatility of the press-imprinted technology for the development of well-defined and robust transducers exclusively based on them (CBNPs), without clean room facilities. Moreover, the coupling of CBNPs transducer/microfluidic chip has led to excellent results. In fact, CBNPs transducer films exclusively supported the electrochemical analytes transduction bringing to excellent microfluidic performance, offering low detection potentials and negligible surface fouling.

These novel CBNPs press-transferred transducers are entering with important roles into the micro and nanotechnology scenes expanding new frontiers in the food analysis and health sector, being an excellent alternative to common approaches in the field.

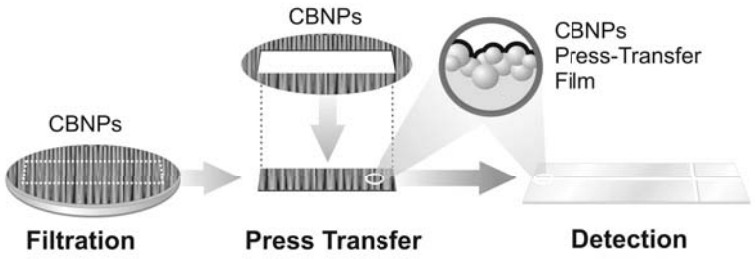

Figure 1. CBNPs film fabrication scheme for microchip detection.

Acknowledgments

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Influence of preparation conditions on structural and mechanical properties of SPEEK membranes for PEMFCs.

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Proton exchange membrane fuel cells (PEMFCs) are a promising technology for clean and efficient power generation. This technology uses a polymeric membrane as electrolyte. As consequence, a lot of research activity has been focused on different types of proton conducting membranes based on polymeric matrices and, among them, sulphonated poly-ether-ether-ketones (hereafter: SPEEK) are interesting low cost materials. Important literature has been dedicated on this class of polyelectrolyte but some problems are still to be overcome such as its excessive swelling at temperatures higher than 80°C, with consequent drop of mechanical properties and reduction of its lifetime. Therefore, it was of interest to evaluate the effect of the preparation conditions (e.g.: choice of casting solvent, drying temperature and post casting treatment) on the structural and mechanical properties of the SPEEK membranes. In this work, SPEEK membranes were prepared by a solvent casting method using a few solvents such as DMA, DMF and NMP and dried at two different temperatures: room temperature for 3 days or 50°C for 1 day. Compared to the membranes dried at 50°C, the membranes dried at room temperature showed enhanced mechanical properties and exhibited reduced swelling, which took place preferably on thickness. DSC measurements carried out on membranes highlighted different microstructure within the polymer matrix, as indicated by the presence/absence of endothermic peak centred around 220°C related to the melting of semicrystalline entities preformed in the membranes[1]. Based on these experimental data, both the drying step and the casting solvent seem critical for structure development and final membrane's performance. Main results are shown in figure 1:

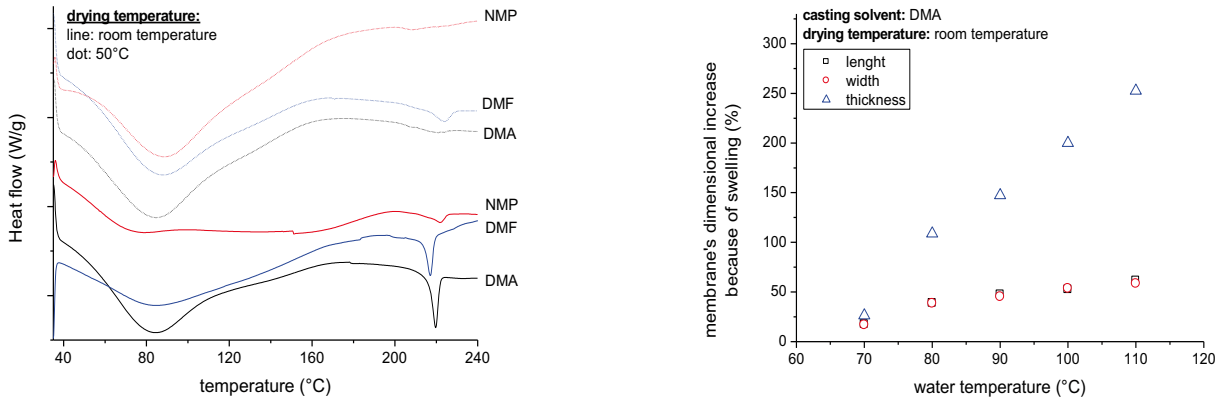

Figure 1. On the left: DSC first scan of SPEEK membranes prepared by varying casting solvent and drying temperature. On the right: anisotropic swelling behaviour observed on rectangular shape membrane.

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Additivi inorganici ritardanti di fiamma non alogenati: idrossido di magnesio naturale ed idrossido di alluminio prodotti per macinazione.

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I materiali organici sono per natura combustibili, ma l'infiammabilità di un materiale polimerico non è una proprietà intrinseca, per cui è possibile cambiare la reazione al fuoco di un materiale cambiandone la sua composizione, ad esempio introducendo un additivo ritardante di fiamma. L'autoestinguenza dei polimeri è spesso ottenuta aggiungendo composti contenenti elementi quali alogeni , azoto o fosforo al materiale polimerico, ma i prodotti della combustione sono composti tossici come acidi alogenidrici, HCN e tossine. Per questo motivo, negli ultimi decenni, la comunità scientifica ha focalizzato la ricerca sullo sviluppo di sistemi di ritardanti di fiamma "green" in grado di ridurre al minimo i fumi tossici e i rischi ambientali quali gli idrossidi inorganici. Idrossidi di alluminio e magnesio (ATH e MDH) sono i prodotti più efficaci: la loro reazione al fuoco risulta essere una decomposizione fortemente endotermica con rilascio di acqua sotto forma di vapore (Figura 1).

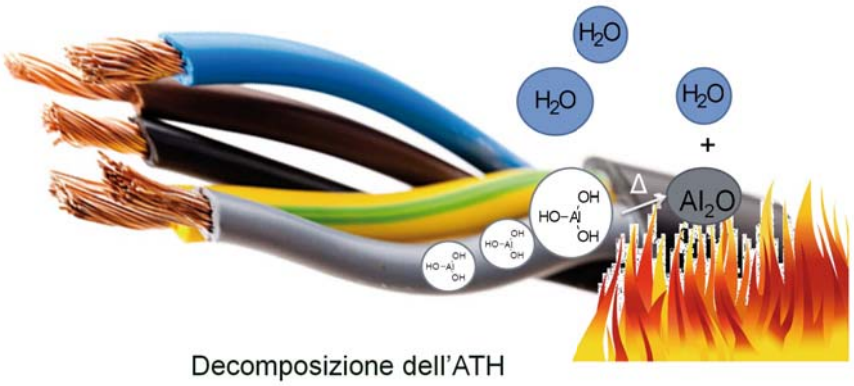

Figura 1

A questo proposito, la Nuova Sima srl è stata un pioniere nella produzione di MDH naturale (Hydrofy) ottenuto dalla macinazione della brucite minerale.[1] La Nuova Sima srl produce anche ATH (Alufy) macinando un prodotto intermedio del processo Bayer, che ha un minore impatto ambientale rispetto all'idrossido di alluminio sintetico. L'attività di ricerca che vede coinvolta l'Università degli studi di Camerino e la Nuova Sima è centrata sullo sviluppo di nuovi trattamenti superficiali con lo scopo sia di migliorare la compatibilità tra tali cariche minerali e i polimeri, sia di ottimizzare l'effetto sulle proprietà meccaniche ed elettriche.

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From Dithio to Monothiocarbamates: New carbonic Anhydrases Inhibitors Possessing Intraocular Pressure Lowering Activity

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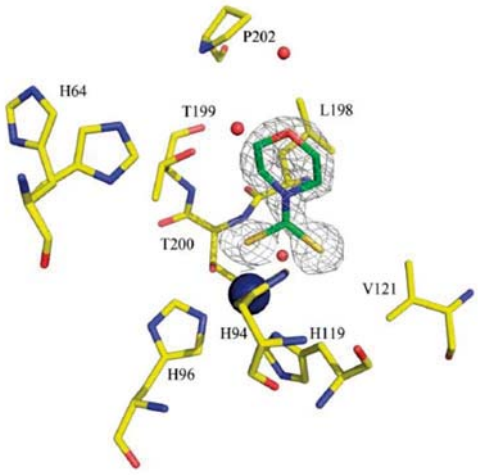
Abstract: Dithiocarbamates (DTCs), Monothiocarbamates (MTCs) and Xantates (XTCs) were prepared and investigated in vitro as carbonic anhydrase (CA, EC 4.2.1.1) inhibitors.
Their binding modes were assessed by means of X-ray crystallization experiments of their adducts with CA II as well as of molecular modeling techiniques.
Furthermore, a selection of DTCs, MTCs and XTCs were evaluated in a normotensive glaucoma rabbit model for their intraocular pressure (IOP) lowering effects, and showed interesting activity.



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Reusability of Chloroperoxidase immobilized on polysaccharide-coated magnetic nanocapsules

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Chloroperoxidase *from Caldaromyces fumago* (CPO) is an aloperoxidase; it is a highly versatile enzyme that catalyzes different reactions, many of them of industrial interest, i.e. sulfoxidation, hydroxylation and epoxidation. However mechanical and oxidative stress cause enzyme deactivation limiting its applications. Enzyme immobilization onto solid supports represents one of the most attractive methods to overcome these drawbacks; therefore CPO is considered a suitable enzyme for the development of enzymatic immobilization systems that can bring to high enzymatic reusability.
In this regard, several CPO immobilization studies have been conducted, for example physical adsorption on amino-agarose gel[1] or covalent attachment on chitosan membranes[2].
Previous studies of our research group demonstrated that CPO entrapment in silica matrices lead to high recyclability of immobilized CPO especially in silica doped with polyethylene glycol 200[3] and polysaccharides[4].
Magnetic nanoparticles are employed in different areas such as biotechnology, biomedicine, environment and engineering; for this reason they represent a forefront research field[5]. Enzyme immobilization on magnetic support is quite investigated topic, but very few works talk about CPO immobilization on magnetic system[6], particularly regarding CPO immobilization on magnetic nanoparticles[7].
Taking into account the stabilizing effect of chitosan and the reusability obtained in the past, in the present work, the efficiency of CPO immobilized in chitosan shell of magnetic nanocapsules was studied, in order to have good enzymatic activity, reusability and, at the same time, to obtain an easy recovery system for the use on a large scale. For this purpose, the polymeric shell of nanocapsules was optimized and four different kinds of magnetic nanocapsules have been developed, using both chitosan, sodium alginate or their combination, with the aim to highlight the most suitable system of enzymatic immobilization to have good CPO efficiency.

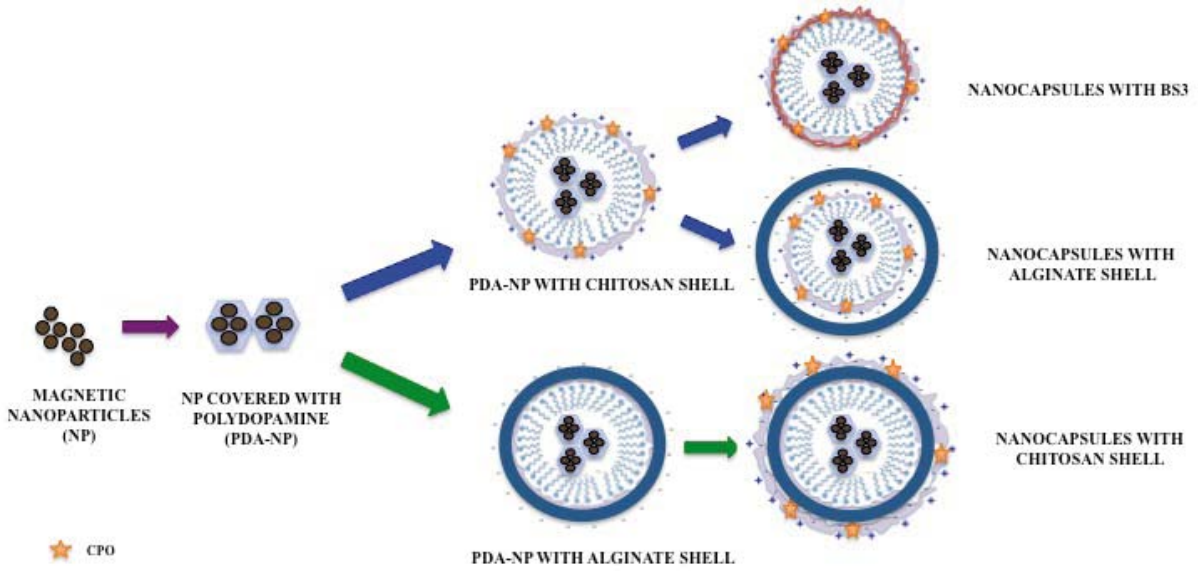

Fig.: Different kinds of magnetic nanocapsules

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E-LEARNING E STILI DI APPRENDIMENTO A SUPPORTO DELLA CHIMICA

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A partire dall'A.A. 2016/17, il test d'ingresso obbligatorio sulle conoscenze minime (D.M. 270/04, art. 6, comma 1) per il corso di studio in Biologia della Nutrizione (LBN) dell'Università di Camerino (UNICAM) verte oltre che sulla Matematica anche sulla Biologia e Chimica. Una adeguata preparazione in queste discipline è utile per intraprendere il corso senza impatti negativi. Nel caso in cui l'esito del test sia negativo, vengono attribuiti degli Obblighi Formativi Aggiuntivi (OFA) che possono essere colmati attraverso Corsi di Integrazione, al termine dei quali lo studente deve sostenere un nuovo test.

L'inserimento della Chimica nel test d'ingresso è un passo importante che promuove il valore di questa disciplina nel contesto del corso, vista la sua propedeuticità per altre materie come Chimica Organica, Biochimica e Citologia e rappresenta una delle azioni messe in campo per contrastare gli abbandoni e migliorare la qualità del corso.

Parallelamente, una studentessa di dottorato in Didattica delle Scienze ha focalizzato il suo interesse sugli stili di apprendimento e, in collaborazione con i Servizi di Orientamento e Tutorato, ha attivato ricerche ed iniziative utili per sostenere gli studenti nell'apprendimento.

La modalità in cui avviene l'apprendimento, fulcro della ricerca, evidenzia il carattere personale e multidimensionale del processo di acquisizione delle conoscenze. Tale modalità più conosciuta come "stile di apprendimento" si riferisce al fatto che ogni individuo, nell'atto di apprendere, sviluppa una procedura legata alle proprie predilezioni e attitudini.

Nell'A.A. 2015/16, il gruppo di ricerca ha redatto un'indagine per rilevare le difficoltà riscontrate dalle matricole al termine del primo semestre, unita a un questionario per tracciare un profilo dei loro stili di apprendimento. Da questa indagine, a cui hanno risposto 87 studenti su 149 iscritti, emerge che il 56% dei partecipanti considera la Chimica una materia difficile da comprendere, problematica da studiare e per la quale chiedono esplicitamente un supporto specifico. Nello stesso anno l'esame di Chimica è stato superato solo dal 25% degli studenti che hanno riportato un voto medio pari a 26/30. Sulla base della difficoltà riscontrata, troppo spesso gli studenti decidono di non affrontare questo esame e lasciarlo tra gli ultimi, con inevitabili carenze di base che si ripropongono per tutto il percorso di studio.

Le ricerche avviate nel campo degli stili di apprendimento, come supporto dell'orientamento e del tutoraggio di Chimica[1], ci hanno spinto a progettare e proporre percorsi condotti con la metodologia *blended learning*. Questa metodologia di formazione flessibile, in presenza e on line, favorisce lo studente a riconoscere i propri stili di apprendimento e ad operare un focus metacognitivo, ovvero imparare a riflettere su se stesso. Gli strumenti offerti dalla piattaforma MOODLE dell'Ateneo (test, chat, forum, wiki) gli permettono di esercitarsi con le strategie che meglio si coniugano ai suoi approcci personali o che lo aiutano a svilupparne di nuovi. In

linea con gli obiettivi del Piano Lauree Scientifiche e sulla base del valore riconosciuto alla trasversalità, gli interventi sono stati condotti in parte anche come azione del progetto nazionale PLS di Biologia e Biotecnologie 2014/16.

Dopo i buoni risultati ottenuti da queste prime esperienze, stiamo configurando anche il Corso di Integrazione di Chimica in modalità *blended learning*. Tale corso ha dunque come premessa l'analisi degli stili di apprendimento dello studente, attraverso un questionario chiamato CAMEA40[2], tradotto dalla Dott.ssa Pulcini e testato dal gruppo di ricerca. I risultati del questionario aiutano a riflettere sui propri metodi di studio, focalizzando le strategie che possono sostenere l'auto-apprendimento dello studente[3].

Da dove derivano queste difficoltà degli studenti verso la Chimica? Forse il problema, come già evidenziato in precedenti lavori[4], risiede negli stili di apprendimento impiegati dagli studenti. Gli stili preferiti dal campione di matricole analizzate sono il riflessivo e il teorico, seguiti dal pragmatico e dall'attivo. Secondo gli studi fatti, coloro che superano l'esame di Chimica con voti più alti hanno una preferenza elevata per gli stili pragmatico e attivo: ciò è confermato dalle prove orali, nelle quali riescono a collegare con semplicità la teoria alla pratica, ottenendo ottimi risultati nelle domande sulla Chimica legate alle esperienze concrete.

Il Corso d'Integrazione di Chimica si articolerà in 3 incontri seminariali in presenza e in 10 moduli disponibili sulla piattaforma. Gli incontri seminariali sono utili per stabilire un rapporto diretto con il docente presente sulla piattaforma, esporre le nozioni di base della Chimica, ascoltare le osservazioni degli studenti e spiegare la struttura del percorso E-learning. I vari moduli propongono brevi lezioni video, letture di approfondimento, link e attività varie (test, forum) modulate sugli stili di apprendimento. Sebbene incentrato sulla Chimica, l'intervento complessivo mira comunque alla conoscenza e al miglioramento dei metodi di studio, e ha quindi un riflesso positivo sull'intera carriera accademica.

Gli stili di apprendimento possono offrire un ottimo approccio per la costruzione di un corso che vada incontro alle esigenze personali di ogni studente: essi permettono, a seconda degli stili dell'individuo, di riconoscere le strategie più efficaci per sostenerlo nell'apprendimento. Il nostro gruppo di ricerca si propone quindi di sperimentare/valutare un corso E-learning di Chimica anche come supporto sostenibile alla didattica curricolare.

In conclusione, gli stili di apprendimento vengono utilizzati, in modo innovativo, come supporto alle strategie per uno studio e insegnamento più efficaci, rappresentando un importante progresso metodologico, che offre preziosi suggerimenti e applicazioni pratiche di elevato impatto. Attraverso l'identificazione degli stili, studente, docente, contenuto e contesto aumentano le possibilità di avvicinarsi, di trovare uno spazio comune.

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Magnetic Resonance techniques powerful tools for antioxidant activity investigation in supramolecular assemblies.

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The advantage of the magnetic resonance methods is the ability to give information about processes at the atomic level selecting out, of total magnetic susceptibility, the particular contribution of interest. Both Nuclear Magnetic Resonance (NMR) and Electron Paramagnetic Resonance (EPR) are non-destructive analytical tool that enables to investigate molecular structure, measure relative and absolute concentrations and intermolecular interactions occurring among active compounds.

This work was aimed at explore the antiradical activity of some antioxidant, like oleuropein, tyrosol and hydroxytyrosol,[1] both in solution and in emulsion by the ability of them to quench the Fremy's salt (potassium nitrosodisulfonate). In fact, EPR technique is very suitable for describing and measure the radical-scavenging processes[2] and NMR spectroscopy is one of the most convenient methods for simultaneous monitoring of changes in aggregate morphologies of interaction between components.

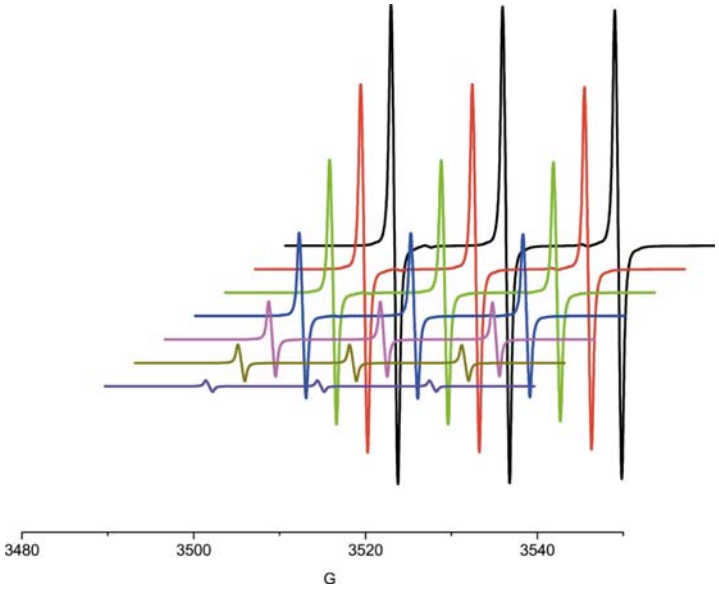

Figure: The scavenging effect: EPR signal of Fremy's salt as function of antiradical concentration.

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Progettazione di peptidi ciclici agonisti misti μ/δ oppioidi

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I farmaci oppiacei sono largamente usati per controllare il dolore, tuttavia essi presentano molte limitazioni dovute ai loro ben noti effetti collaterali, come lo sviluppo di tolleranza, ~~e~~ dipendenza e depressione respiratoria.
Inoltre la loro efficacia nel controllare il dolore cronico e neuropatico è molto scarsa.
Negli ultimi anni, alcuni studi hanno evidenziato la possibilità che i recettori oppioidi possano aggregarsi per formare omo- ed etero dimeri, come ad esempio il complesso eterodimerico costituito dai recettori μ e δ.
La loro simultanea attivazione potrebbe quindi determinare un effetto sinergico e un potente effetto analgesico a dosi minime di farmaco.[1]
Il nostro gruppo di ricerca si è dedicato negli ultimi anni alla sintesi di nuove molecole partendo da due famosi peptidi oppioidi: la bifalina (Tyr-(D)Ala-Gly-Phe-NH-)$_2$ ed il DPDPE (Tyr-*c*[(D)Pen-Gly-Phe]-(D)Pen-OH).
La Bifalina ha una elevata attività antinocicettiva, si lega ai recettori oppioidi μ e δ in range nanomolare di concentrazione ed attiva la proteina G efficacemente.
E´ stato imostrato che tale molecola attraversa la barriera ematoencefalica, risultando attiva per via endovenosa, anche se in larga parte, subisce una disattivazione da parte di molti enzimi presenti nell'organismo.
Infatti la sua attività è più bassa della morfina per via endovenosa, ma risulta centinaia di volte più attiva quando somministrata direttamente per via intratecale o intracerebroventricolare (*i.c.v.* o *i.t.)*.[2]

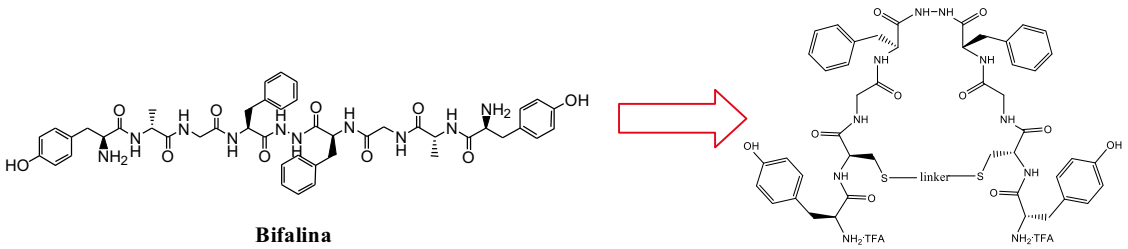

Figura 1. Bifalina ed analoghi ciclici della Bifalina.

Fino ad ora molti analoghi della bifalina e del DPDPE sono stati sintetizzati con ottimi risultati sia a livello di aumentata stabilità metabolica, sia come miglioramento dell'affinità per i recettori oppioidi.
Le modifiche principali effettuate dal nostro gruppo di ricerca sulla bifalina sono riassunte nei seguenti punti:
1) Sostituzione del ponte idrazinico con diverse diamine come la piperidina ed aril-diammine.[3]
2) Uso di aminoacidi della serie beta.[4]
3) Sostituzione della fenilalanina in posizione 4,4' con *p*-fluoro-fenilalanina.[5]

4) Progettazione di diversi analoghi ciclici mediante la sostituzione dei residui di (D)-Alanina in posizione 2,2' con residui di (D)-Cisteina, (D)-Penicillamina, (D)-Allil-Glicina.[6]
5) Ultimamente, abbiamo usato un differente tipo di linker (isomeri del dibromo-xilene) capace di reagire con i due gruppi tiolici presenti in catena laterale degli aminoacidi, per chiudere un ciclo.

La valutazione degli effetti biologici di queste modifiche strutturali è stata effettuata inizialmente mediante saggi *in vitro,* in seguito rilevando l'attivazione della proteina G ed infine attraverso saggi *in vivo* su ratti mediante Hot Plate Test e Tail Flick Test.
L'impiego di un linker bidentato come il dibromo-xilene ha permesso di generare nuovi peptidi ciclici con elevata stabilità metabolica ed altissima affinità per i recettori μ e δ, rivelandosi un valido approccio per la ricerca di agenti antinocicettivi esenti dagli effetti collaterali tipici dei oppiacei.

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Polybrominated diphenyl ethers (PBDEs) in the environment: Source and Environmental fate

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Polybrominated diphenyl ethers (PBDEs) have been commonly used as flame retardants in a wide range of manufactured products including furniture, textiles, carpets, building materials, electronics, furnishings, motor vehicles, polyurethane foams and electronic circuit boards.
They have been mainly used in three commercial formulations named according to their average degree of bromination: penta- (mostly penta- and tetra-BDE congeners), octa- (mostly octa- and hepta-BDE congeners) and deca-BDE mixture. Currently, deca-BDE accounts for over 80% of the total PBDE production (1, 2). Tetra-, penta-, hexa-, hepta- and octa-BDEs have been named persistent organic pollutants (POPs) under the Stockholm Convention (5). Environmental levels of PBDEs were continuously increasing until the beginning of the 2000s, when declining trends were first observed (4, 6). These congeners are ubiquitous in the environment, and thereby transferred to humans via the food chain. Heavier BDEs, such as BDE-209, are less stable and can degrade thermally, upon exposure to UV light, or through several biotic mechanisms to form lighter and more toxic BDEs (3, 4). Increasing concentrations in human tissues and environmental samples, even from remote areas, have focused worldwide attention on the potential health effects of PBDEs. Data on animal exposures indicate that some PBDEs are toxic or can cause endocrine disruption (1). Because of toxicological effects evidenced, penta- and octa-BDE mixtures have been banned in Europe and United States and were substituted in their application by deca-BDE, that not evidenced direct toxicity but has the tendency to degradation. Restrictive measures have been taken in this regard also sanctioned by the European Court of Justice (1 July 2008).
In recent years, new brominated flame retardants have been introduced in the market, in particular organo-phosporous compounds (i.e. Trischloropropyl phosphate (TCCP) or other brominated compounds, such as TBBA (Tetrabromobisphenol A). However, studies on their toxicological effects, environmental distribution and fate are still in progress; and, the synthesis of new molecules is considered a new challenge.
In the last ten years, our research group in Florence has focused its studies on the occurrence, levels and distribution of PBDEs in different environmental matrices (sludge, soil, water, biota, food, etc.) and in different regions, developing or improving extraction and purification techniques for different environmental media and combining classic (i.e. GC-MS techniques) to innovative, fast and cost effective instrumental techniques (i.e. Electrochemical Immunoassay) (7).
A overview of the principal studies on PBDEs will be presented.
The presence, level and composition profile of eight PBDEs was studied in various wastewater treatment plants (WWTPs). For the first time in Italy, PBDEs were determined in sludge (8) and air samples collected at different sites in and around two WWTPs located in central Italy (Martellini et al., 2012) in order to estimate the influence of the plants in the surrounding air quality. We also evidenced that the classic wastewater treatment processes are not able to efficiently remove these molecules from their effluents; thus new materials, as well as zeolites, were tested to remove these contaminants (9) and experimental studies on the potential of bacteria aerobic strains to reduce PBDEs in output sewage sludge were carried out on a pilot scale.

Recently, atmospheric occurrence and gas-particle partitioning of PBDEs in an industrialised and urban area of Florence, Italy was also investigated (10).
Our research group also received national and international funds to assess the levels, distribution, potential sources and fate of PBDEs in remote and pristine areas, such as Arctic and Antarctica, and, in order to achieve these aims, organisms (11), air (12) and seawater samples (13) were analyzed.
Moreover the human exposure through the diet was studied determining the occurrence of PBDEs in foodstuffs (6). Finally, a new approach of marine environment biomonitoring has been applied through the use of amphipods to assess the presence of flame retardants and PCBs in coastal areas (14, 15).

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IDENTIFICATION, HIT EXPLOSION, AND MECHANISM OF ACTION INVESTIGATION OF PYRIDOBENZOTHIAZOLES AS ANTI-FLAVIVIRUS COMPOUNDS

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Belonging to the *Flaviviridae* family, Flavivirus genus comprises more than 70 RNA viruses pathogenic to humans and usually transmitted by vectors such as mosquitoes and ticks.[1] In the past, flavivirus infections were classified by the World Health Organization as neglected tropical diseases, but on the basis of environmental, demographic, and ecological evidences scientific community believes that flaviviruses could represent a global health emergency in the future.[2] Dengue, West Nile, Yellow fever, Japanese enchephalitis, and the emerging Zika viruses are now considered important pathogens.[3]
Flaviviruses produce from mild to severe symptoms and in some cases lead to hemorrhagic fevers and encephalopathies, including microcephaly in human embryos induced by Zika. An effective and specific therapy against these viruses is currently not available and moreover the broad-spectrum antiviral compound ribavirin is ineffective to treat flavivirus infections.[4] Similarly to HIV and HCV, the targeting of the viral polymerases is undoubtedly a valid strategy to find new anti-flavivirus agents.

In this regard, we have decided to re-task our focused library of HCV NS5B RdRp inhibitors, consisting of about 200 published[5] and unpublished compounds, toward flavivirus NS5 RdRp. First, we screened *in silico* such library against DENV3 RdRp[6] and submitted the top-scoring compounds to biological evaluation; this approach led to the identification of an unpublished pyridobenzothiazole derivative as non-competitive micromolar RdRp inhibitor. Notably, it was also able to selectively inhibit flaviviruses (DENV1-4, WNV, and YFV) replication with IC_{50}s in the micromolar range. Co-crystal structure of the hit compound bound to the DENV3 RdRp revealed a binding site consistent with a competitive inhibition rather than allosteric modulation of the enzyme. In parallel, a first round of medicinal chemistry hit optimization led to a new promising analogue, that was used as chemical probe to investigate in cell different aspects of this compound class such as: (*i*) the viral specificity against flavivirus family, (*ii*) the action on different permissive host cells, and (*iii*) the effective RdRp involvement in the mode of action for this chemical series.

In this communication, results derived from the multidisciplinary approach employed in this research program will be reported.

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NOVEL ZWITTERIONIC DEEP EUTECTIC SOLVENTS: CHARACTERIZATIONS AND SYNTHETIC APPLICATIONS

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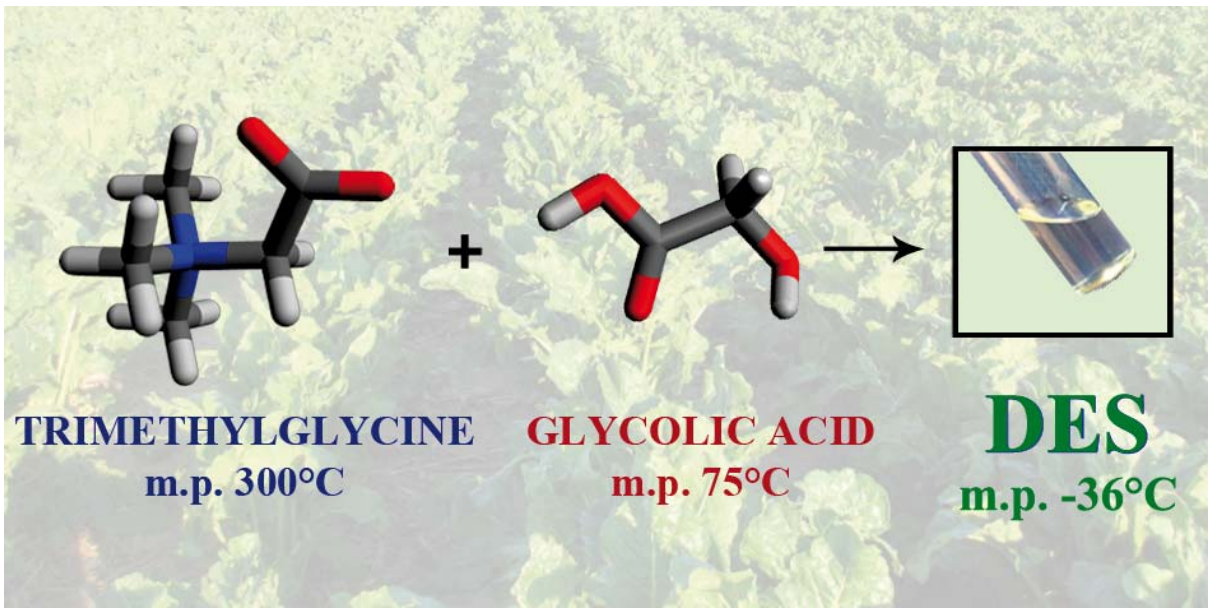
The search for low toxicity reaction media has been investigated thoroughly, especially to find alternatives to organic solvents. One of these alternatives is represented by Ionic Liquids (ILs) formed by organic cations and organic or inorganic anions, which are liquid at temperatures under 100°C[1]. These reaction media have many advantages compared to typical organic solvents such as low vapour pressure and high recycle capability. Unfortunately ILs show also many "green" disadvantages because of their low biodegradability and low biocompatibility and therefore low sustainability; moreover the synthesis and purification of these media often requires extensive use of organic solvents. For these reasons, more biocompatible novel systems have gained relevance in recent years, like Deep Eutectic Solvents (DESs). DESs are a novel family of organic media generally liquid at temperatures lower than 100°C. DESs show chemico-physical properties similar to the traditionally used ionic liquids; however they are less toxic and more biodegradable[2]. DESs can be prepared by mere mixing high-melting-point quaternary ammonium or phosphonium salts with neutral compounds, which are able to form hydrogen-bond interactions, as alcohols, amides, carboxylic acids, phenols, polyols or carbohydrates. The strong interaction between the hydrogen-bond donor compound and the anion, provided by the salt, leads to a considerable reduction in the melting point of the mixture.



In this work we report the preparation and the characterization of novel classes of zwitterionic DESs. The first class is represented by mixtures of trimethylglicine with aromatic and aliphatic carboxylic acids[3]; the second class is formed by (1S)-(+)-10-camphorsulfonic acid (CSA) and differently structured sulfobetaines with aliphatic, aromatic and amphiphilic

moieties, and they are liquid at room temperature (RTDESs)[4]. A DES from this second class (3-(cyclohexyldimethylammonio)propane-1-sulfonate and CSA mixture) was successfully used both as reaction media and catalyst in Carbon-Carbon bond formation via Claisen-Schmidt reaction[5]. The advantages of the use of this DES in this probe reaction are represented by: the green properties of the media and its low toxicity; the absence of harmful acids to catalyse the aldol condensation because of the camphorsulfonic acid composing the DES mixture; the recycling and the re-use of the DES in subsequent reaction cycles; the mild conditions and the excellent conversions and yields observed.

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POSTER

NOVEL Sn(IV) AND Ru(II)-ARENE COMPLEXES CONTAINING ACYLPYRAZOLONES-BASED LIGANDS: SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL STUDY

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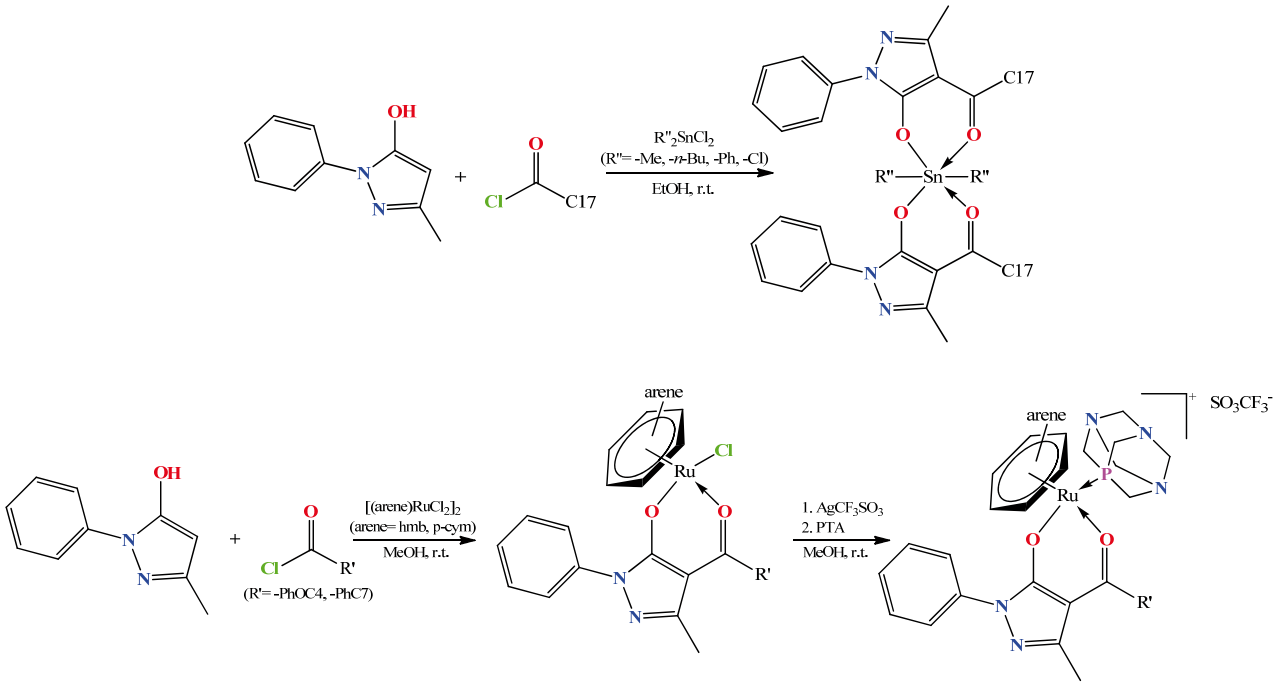
Acylpyrazolones are a class of β-dicarbonyl ligands bearing a pyrazole fused to the chelating arm. The acyl moiety greatly affects the binding properties of acylpyrazolones. This family of molecules displays interesting anti-inflammatory[1], anticancer[2], antimicrobial[1], insecticidal[3] and fungicidal[3] properties. They have also been used for the metal extractions and nowadays they are mostly investigated as ligands toward metal acceptors.[4,5]

In the last decades many organotin(IV) complexes were used as antifouling agents and they have also applications as biocides[6]. Ruthenium(II)-arene complexes have found important applications in catalysis[7] and they have recently attracted a growing interest for their antiviral, antibiotic and anticancer properties[8].

In this work, we report the synthesis of three new acylpyrazolone ligands, namely 1-(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)octadecan-1-one (HQ^{C17}), (4-butoxyphenyl)(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methanone (HQ^{PhOC4}) and (4-heptylphenyl)(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl)methanone (HQ^{PhC7}) respectively, as well as the preparation, structural characterization, thermal and biological investigation of their organotin(IV) and areneruthenium(II) complexes. In detail, we were able to isolate $[(Q^{C17})_2SnR_2]$ complexes (R= -Me, -*n*-Bu, -Ph, -Cl) and neutral and ionic [(arene)Ru(Q)Cl], and [(arene)Ru(Q)(PTA)]SO_3CF_3 complexes, respectively (Q = Q^{PhOC4}, Q^{PhC7}; arene = *para*-cymene (cym) or hexamethylbenzene (hmb), PTA = 1,3,5-triaza-7-phosphaadamantane) (**Scheme 1**).

All complexes have been fully characterized by melting point, elemental analyses, FT-IR, ESI-MS, TGA, ^{1}H-NMR, ^{13}C-NMR, ^{119}Sn-NMR and ^{31}P-NMR spectroscopy.

The organotin(IV) $[(Q^{C17})_2SnR_2]$ complexes are stable both in air and in solution, soluble only in chlorinated solvents and DMSO. The TGA study reveals that they are all stable up to 300 °C. The ^{119}Sn-NMR spectra show the presence of more than one species in solution for complexes $[(Q^{C17})_2SnPh_2]$ and $[(Q^{C17})_2SnCl_2]$. They have a good antioxidant activity and are able to interact with BSA protein of blood.



Scheme 1

The areneruthenium(II) complexes are stable both in air and in chlorinate solution and acetonitrile, where those with PTA ligand are ionic, with the triflate groups outside the ruthenium coordination sphere. The ^{31}P-NMR spectra confirm the stability of the ionic complexes in solution. They show also a quite good ability to interact with BSA protein of blood. X-Ray diffraction studies for some complexes and investigation of their anticancer activity are in progress.

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Sintesi di nuovi leganti e complessi di oro(I) e applicazioni in catalisi

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L'intrinseca π-filia di complessi e sali di oro cui è legato il successo di questi catalizzatori quali promotori di peculiari trasformazioni chimiche ha favorito e stimolato in anni molto recenti lo sviluppo di nuovi leganti chirali per questo metallo al fine di realizzare trasformazioni enantioselettive. Le difficoltà nel disegno di catalizzatori chirali efficienti di oro(I) sono legate alla coordinazione lineare di questo metallo che richiede la costruzione di leganti in grado di includere e schermare efficacemente l'atomo di oro rendendo accessibile il centro metallico con una disposizione spaziale utile per la catalisi asimmetrica. Questa difficoltà è stata superata costruendo leganti dalla struttura articolata, spesso sintetizzabili attraverso complessi processi a più stadi e certamente molto onerosi in termini di tempi e costi e di modularità del legante.[1] Negli ultimi anni, nell'ambito della catalisi metallica enantioselettiva, sono emerse nuove classi di leganti che contengono motivi strutturali ispirati a building blocks chirali di origine naturale. Tra questi vi sono proteine o peptidi utilizzati come tali, oppure leganti sintetici modificati con l'introduzione di strutture di origine naturale.[2] L'utilizzo di piccoli peptidi, in grado di mimare l'attività di metalloenzimi naturali, presenta indubbi vantaggi quali la facilità nella sintesi e la possibilità di effettuare modifiche puntiformi nella sequenza, al fine di migliorare l'attività catalitica e la capacità di coordinazione. In questo ambito e tenendo in considerazione quanto già riportato in letteratura sull'efficienza di leganti ispirati a building blocks di origine naturale sono state disegnate alcune piccole sequenze peptidiche, caratterizzate dalla presenza di un β-turn indotto dalla presenza di amminoacidi non naturali e di catene amminoacidiche laterali in grado di fungere da leganti per l'oro, Figura 1.

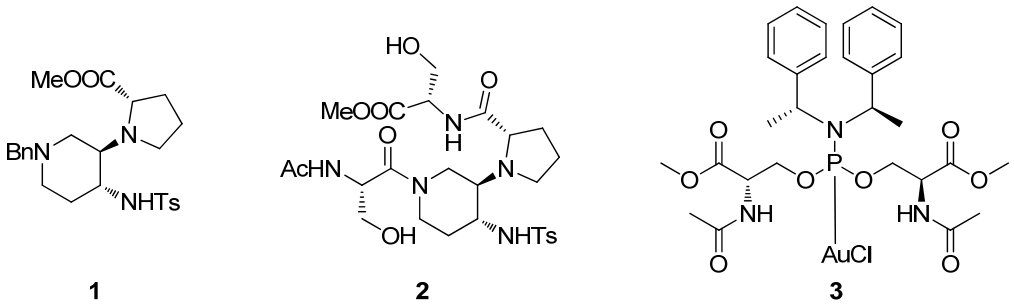

Figura 1

La sintesi dell'amminoacido non naturale **1** e del corrispondente tetrapeptide **2** verranno riportate accanto alla sintesi e alle prime applicazioni catalitiche del catalizzatore modello **3**.

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Mild AgOTf Catalyzed Synthesis of 1-Carbosubstituted-isochromenes

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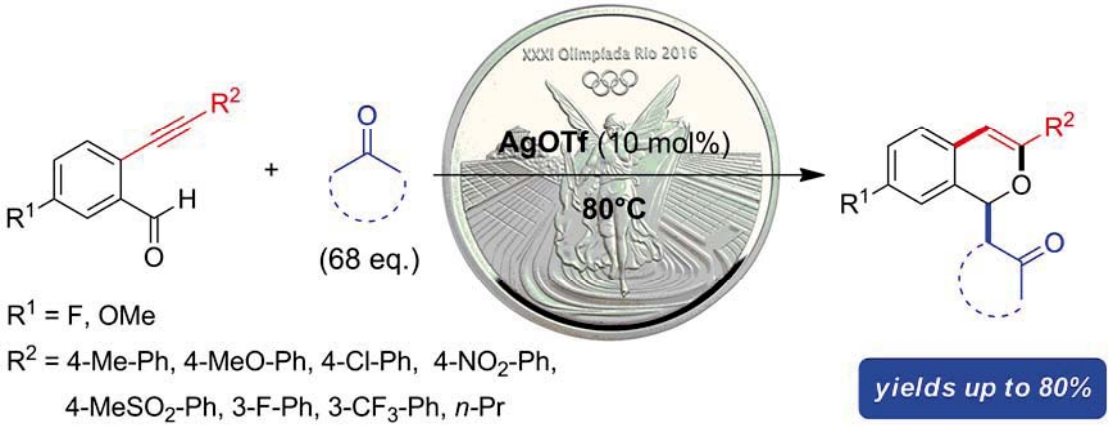
One of the most efficient methods for the construction of 1-substituted isochromenes (and related heteroaryl compounds such as pyrano[4,3-b]pyridines) is the metal catalyzed regioselective domino cycloisomerization/nucleophilic addition reaction of a properly substituted 2-alkynyl(hetero)arylaldehyde in the presence of a suitable nucleophile.[1] The reaction with oxygen nucleophiles is the most studied and several metal catalyst, i.e., Pd(II),[2] Cu(I),[3] Ag(I),[4] Au(I)[5] and In(III),[6] demonstrated to be effective for synthesis of 1-alkoxyisochromenes. Conversely, the reaction with carbon nucleophiles, and in particular with enolizable carbonyl compounds, is relatively less investigated.[7] In connection with our ongoing interest in the development of silver catalysed domino approaches involving alkyne derivatives,[8] we report here a silver catalyzed domino approach to isochromenes starting from 2-alkynyl(hetero)arylaldehydes and enolizable carbonyl compounds. The reaction yields range from fair to very good. The reaction mechanism is also investigated and the formation of by-products discussed.



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AN IMPROVED ROUTE TO QUINOLINES FROM α,β-YNONES

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We have previously showed that α,β–ynones **4** are useful starting material for the synthesis of quinolines using various cyclization strategies,[1] whose common feature is represented by the conversion of the triple bond into a *cis*-alkene moiety, followed by cyclocondensation. Conjugate addition of nucleophiles was showed to be a simple and efficient route to convert **4** into 2,4-disubstituted quinolines **5**.[2] Ynones **4** (R = aryl, vinyl) were obtained by a carbonylative Sonogashira coupling under CO atmosphere. We report here an improved approach to **4** that avoids the use of CO and allows also the introduction of R = alkyl (as well as aryl and vinyl). Propargylic alcohols **1**, easily obtained by Grignard reaction, were coupled with **2** to give **3**. Subsequent oxidation with Mn (IV) afforded ynones **4**.

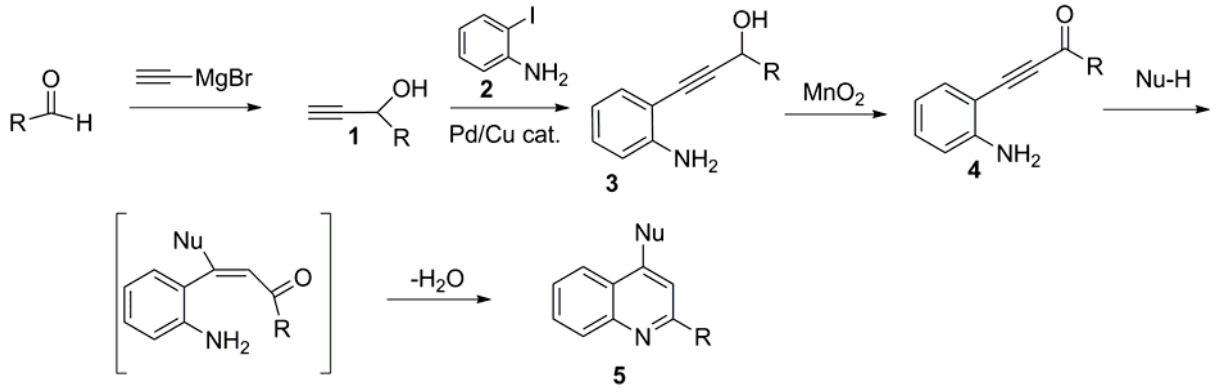

Fig. 1

We have also expanded the range of nucleophiles involved in the subsequent conjugate addition: sulfinate ($ArSO_2^-$) and nitrite anions react with **4** in the presence of NH_4Cl as proton donor, affording interesting 4-nitro [3] and 4-sulfonyquinolines.[4] The former were easily converted to 4-aminoqinolines or 4-hydroxyquinolines, whose preparation through direct conjugate additions of hydroxide ion or ammonia to **2** gave poor results. It must be pointed out that previously reported synthesis of 4-nitroquinolines require activation of quinoline ring as N-oxide, electrophilic nitration and subsequent reduction of N-oxide [3,5]. On the other hand, interest towards 4-sulfonyquinolines originates from the observation that the good leaving ability of sulfonyl group facilitates S_NAr reactions, and this characteristic has been employed in the large scale synthesis of the macrocyclic HCV protease inhibitor BI 201302 [4]

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Addizione palladio catalizzata di ioduri arilici ad alcol propargilici. Sintesi di alcol γ, γ diaril allilici.

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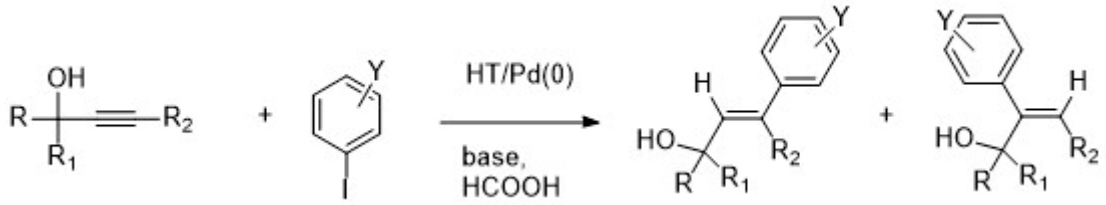
E' noto che la reazione di ioduri arilici con alcoli propargilici variamente sostituiti, in presenza di Pd $(OAc)_2$ $(PPh_3)_2$ piperidina e acido formico, risulta essere una buona via di sintesi degli alcoli γ, γ- diaril allilici[1].

Partendo da queste premesse, al fine di rendere la reazione rispondente agli attuali criteri di sostenibilità, è stato studiato un metodo di sintesi che preveda l'uso di un catalizzatore eterogeneo.

Allo scopo è stata valutata la sintesi di un catalizzatore a base di nanoparticelle di Pd (0) supportate da idrotalciti Mg/Al[2].

Il catalizzatore così ottenuto è stato utilizzato nella reazione precedentemente descritta di ioduri arilici con alcoli propargilici per ottenere alcoli γ, γ-diaril allilici. (Schema 1)



Schema 1

Verranno presentati al Convegno i dettagli e discusse le potenzialità di questa procedura alternativa.

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ADVANCED FUNCTIONAL COATING: STUDY AND RESEARCH TO DEVELOP ANTI-FINGERPRINT COATING FOR INDUSTRY USE

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The coating is superficial covering obtained through chemical compound deposition on surface. This thin film has thickness between 1 μm and 1nm. Nowadays, touch screen displays and glass surface are common in modern appliances and devices such as smart phones. Surfaces routinely touched are contaminated with fingerprints and makes it look dirty. Therefore, the fingerprint problem on the surface is a most pressing issue to be solved by the development of the protective coating materials, which possess hydrophobic and oleophobic (i.e. amphiphobic) properties[1,2]. In the literature materials that show the hydro and oleophobic properties are those based on fluorinated polymers: fluorinated acrylic copolymers [3]; perfluoropolyether (PFPE)[4], fluoroalkylsilane[5]. Fluoropolymers are made of "high tech" materials at very high performance and expensive. Thanks to the presence of C-F bonds the molecules are particularly stable and show a low surface free energy, this prevents the deposition of dirt. The aim of this study is formulate a functional coating with anti-fingerprint property but keeping an easy application and moderate price for industry use. In this work, we report the raw materials selected from different multinational chemical manufacturers. In detail raw materials that have good adhesion on glass, good degree of transparency and gloss, associated with hydro and oleophobic properties; such as perfluoropolyether with different functional groups, fluoroalkyl resin, silicone epoxy resin, fluorocarbon dispersion, mixture of silane and siloxane. From this first tests, the PFPE and fluoroalkylsilane compounds are able to impart outstanding water and oil repellence, friction reduction and anti-dirty properties to the treated surface. The glass surface treated with this compounds result to be easy-clear, however the fingerprint sing remains on surface. Next works will be direct at increase deep porous structures of surface to improve oleophobic and anti-fingerprint properties. The surface texturing will be characterized by deeper valleys, through nano-porous or mesoporous coatings[6]. This coatings can be achieved through sol-gel method, that get involved an inorganic polymerization reaction to form a three-dimensional network. This inorganic-organic hybrids will be obtained with precursors such as organoalkoxysilanes and functionalized oligomers.

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Studio dei diversi stati di ossidazione dei solfuri in soluzione mediante complessi di esacianometallati.

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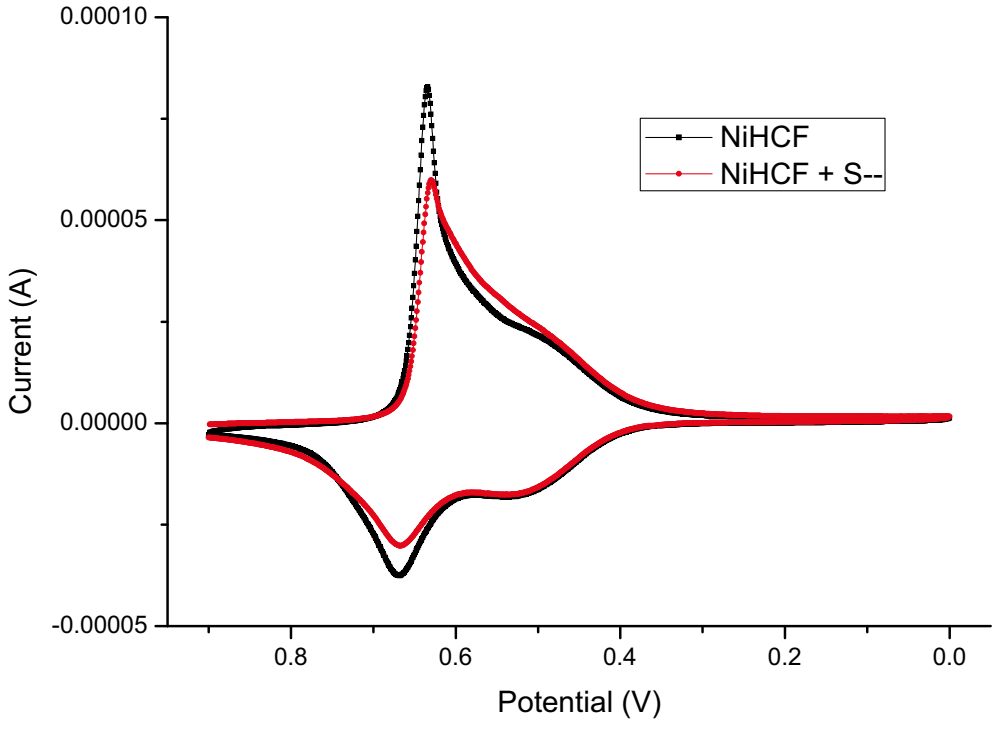
Gli esacianometallati sono una classe di composti studiata in tutto il mondo per la loro elevata duttilità in campi elettrochimici. Si tratta di complessi altamente stabili che presentano caratteristiche di elettrocatalisi ed elettrocromismo. Il capostipite di questa famiglia è l'esacianoferrato di ferro(III) (Blu di Prussia).

La solubilità dei solfuri è influenzata dal pH e la specie più pericolosa di questo equilibrio è l'acido solfidrico uno dei maggiori inquinanti, che favorisce la corrosione dei metalli ed è tossico per gli esseri viventi. Questo lavoro ha lo scopo di voler studiare i diversi stati di ossidazione dei solfuri in soluzione sfruttando le proprietà elettrocatalitiche dei complessi esacianometallati.



Nella figura vengono messi a confronto i risultati ottenuti dell'elettrodeposizione dell'esacianoferrato di nichel e dello stesso complesso a seguito dell'aggiunta di solfuro di sodio, in soluzione neutra.

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The effect of the potential energy surface on vibrational transitions in N_2-N_2 collisions

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Non equilibrium conditions can be the rule in the chemistry of the upper atmosphere, combustion and laser chemistry, and in the chemistry of plasma, especially when the vibrations of diatomic molecules are concerned. In this sense, vibrationally excited molecules and vibration to vibration (VV) energy transfer in N_2-N_2 collisions play a crucial role both in high temperature, as in hypersonic flows in the atmosphere, and in low temperature (gas lasers, plasma reactors) regimes, so that the accurate experimental and theoretical determination of cross sections and rate constants of related processes is a topic of increasing interest [1,2,3].

One of the most efficient approaches to calculated these quantities remains at the date the quantum-classical method introduced and developed by Billing [4], which couples a rigorous quantum mechanical treatment of vibrations and of roto-vibrational coupling and a quasiclassical description of the other degrees of freedom, allowing the calculation of energy exchange probabilities for a large body of state selected processes at a reasonable computational cost.

The accuracy of the results thus strongly depends on the ability of the potential energy surfaces to correctly describe both long and short range interactions which dominate the outcome of the collisions at different temperature regimes.

In this work we compare cross sections and rate constants for VV processes in N_2-N_2 collisions, calculated within a mixed quantum-classical approach in a wide temperature range, using the potential recently adopted in [1], its updated version, obtained by modifying the long range interaction, and the potential energy surface of ref. [3], which includes reactive channels in the description of the interaction.

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Caratterizzazione Elettrochimica e Spettroscopica del $MnFe(CN)_6$

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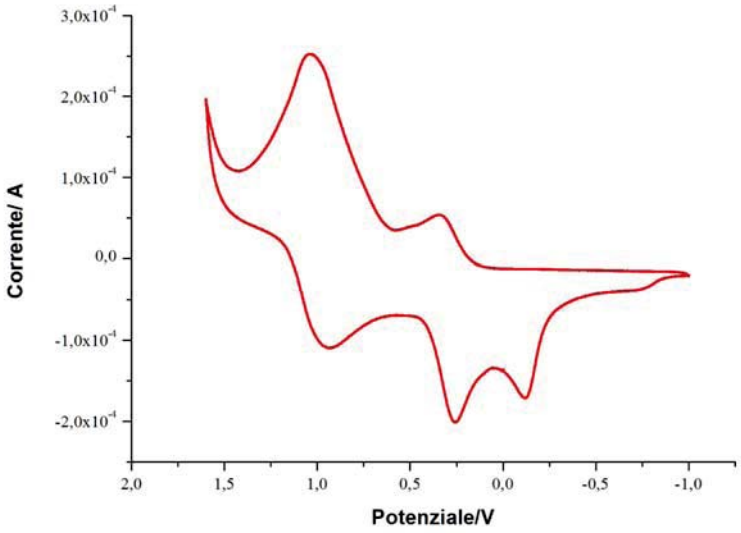
Gli esacianoferrati sono la prima classe di esacianometallati studiati con formula generica $A_xM_y[Fe(CN)_6]^-mH_2O$, dove la M indica un metallo di transizione e A un metallo alcalino, x e y sono I coefficienti stechiometrici e m è il numero di molecole d'acqua nella struttura. Il più importante esempio di questa classi di composti è il Blu di Prussia $Fe_4[Fe(CN)_6]_3$

Questo lavoro è propedeutico alla sintesi e caratterizzazione chimica ed elettrochimica di esacianomanganati misti analoghi del Blu di Prussia a partire dall'esacianomanganato di potassio.[1] Lo studio ha riguardato la caratterizzazione elettrochimica e spettroscopica del composto $MnFe(CN)_6$ e il suo isomero $FeMn(CN)_6$.



In figura è rappresentata la voltammetria ciclica dell'esacianoferrato di manganese depositato su un elettrodo di lavoro in carbone vetroso utilizzando come elettrolita di supporto il Perclorato di Sodio 1M [2]. La risultante elettrochimica è molto complessa a causa dei numerosi stati di ossidazione del Manganese.

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Immobilization and delivery of biologically active Lipoxin A_4 using electrospinning nanotechnology

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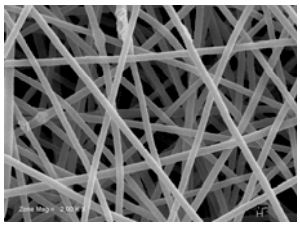
The electrospinning process consists in extruding a polymeric solution through a fine nozzle by means of a strong applied electric field. Electrospun mats possess outstanding features such as small fiber diameters, high specific surface area and high porosity which make them suitable as promising systems for scaffold and drug delivery. In the present study we report on the optimization of the electrospinning process and on the definition of an operating protocol able to provide reproducibly electrospun nanostructured polymeric membranes formed by a blend of poly (D,L-lactide) (PDLLA) and poly (ethylene oxide) (PEO), loaded with Lipoxin (LX)A_4, a lipoxygenase-formed arachidonic acid metabolite with potent anti-inflammatory properties.

Figure 1: SEM image of PEO/PDLLA fibers



These membranes were fully characterized by scanning electro microscopy, differential scanning calorimetry and biocompatibility with human periodontal ligament stem cells (hPDLSCs). These results demonstrate that LXA_4 can be incorporated into biomembranes, which may be useful to combat local inflammation and promote tissue repair in selected clinical settings.

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IN VITRO DIHYDROXYNAPHTHALENE-BASED FUNGAL MELANOGENESIS EXPLORED *VIA* ELECTROSPRAY IONIZATION MASS SPECTROMETRY (ESI MS)

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The term "melanin" embraces a heterogeneous group of polymeric amorphous natural substances without a defined structure shared by animals, plants, bacteria and fungi which represent the key components of the pigmentary system of such organisms. In the last two decades, increasing attention is being focused to exploring and revealing the unique structural, antioxidant, photoprotective and optoelectronic properties of eumelanin biopolymers.[1] Their physical-chemical properties make these natural macromolecules good candidates for bio-inspired soft materials.[2] Recently, a structurally-defined eumelanin-based thin film was used as biocompatible platform for stem cells growth.[3] Notwithstanding that chemistry of both natural and synthetic eumelanin polymers has been investigated,[4] very few studies are present in the literature reporting on allomelanins,[5] which is the most heterogeneous group of natural melanins of non-animal origin.

In the fungal kingdom, the black pigment of ascomycetes fungi derives from oxidation and polymerization of the chromogen 1,8-dihydroxynaphthalene (1,8-DHN), producing 1,8-DHN-melanin-type.[6] Even though the biosynthetic pathway has been studied in detail,[7] the complete structure of the DHN-polymer is not fully elucidated. Very recently, a deeper exploration on the enzyme-mediated polymerization of DHN has been performed on 2,7-DHN, a commercially available structural isomer.[8]

Herein, we report on the comparison between the *in vitro* polymerization of 1,8-DHN and 2,7-DHN under controlled biomimetic conditions, using two different oxidative systems as horseradish peroxidase/H_2O_2 and laccase/air. The poly(1,8-DHN) and poly(2,7-DHN) have been fully characterized by Electrospray Ionization Mass Spectrometry (ESI-MS). The ESI mass spectra of both the polymers show peaks separated by 158 Da, corresponding to the "in chain" DHN unit (MW 160 Da). The ESI MS investigation allowed to detect oligomers in a wide *m/z* range, up to about 5000 Da (i.e. XX-mer) for poly(1,8-DHN) and about 2000 Da for poly(2,7-DHN), corresponding to X-mer. Nevertheless, in-depth UPLC-ESI MS analyses of acetylated reaction mixtures reveal significant differences on the mode of polymerization of such precursors. 1,8-DHN polymerizes *via C-C* coupling of the aromatic nuclei while poly(2,7-DHN) is composed of both *C-C* and *C-O* linked oligomers. This implies that hydroxyl-moieties of 1,8-DHN are not involved in the polymerization while poly(2,7-DHN) builds up using *–OH* groups as well as aromatic carbon.

Some NMR results, which confirm the above described overall structural picture, will be also presented.

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TIMS Measurements of $^{87}Sr/^{86}Sr$ Isotope Ratio in "Pecorino di Farindola" Cheese for Geographical Origin Investigation

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The geographical origin of food is being intensively studied due to increasing food frauds[1-5]. The possibility of using precise measurements of strontium isotope ratios for the geographical characterization of "Pecorino di Farindola", a typical cheese from the Abruzzo region of Italy, has been investigated. 15 authentic samples were analyzed and compared to 26 sample of similar cheese coming from different regions of Italy (Abruzzo, Sardinia and Tuscany). Thermal Ionization Mass Spectrometry (TIMS) was used for the measurements. The technique was able to clearly define a cluster for "Pecorino di Farindola". The strontium isotope ratio resulted to be a valid parameter for the geographical recognition of 73% of the other tested samples (Abruzzo, Sardinia, Tuscany). The relationship between the strontium isotope ratios in Farindola cheese and soils of the region of origin has also been investigated[6].

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Functional Food Supplements: Analysis HPLC/DAD and GC/MS of Short Chain Fatty Acids (SCFAs) in fermented food products

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The common known Gastrointestinal diseases and health issues are caused by imbalances in the microbiota in the large intestine.

A variety of substrates may be metabolized by intestinal microbiome including starch, dietary fibres, simple sugar, sugar alcohols. Multispecies probiotic formulations have shown beneficial effects, they providing competition, inhibiting pathogenic organism and their main function is to breakdown undigested food materials into SCFAs. Although most of the SCFAs are adsorbed in the colon, 10 to 20% are excreted in the faeces[1]. There are several types of SCFAs produced as a result of metabolic activity, including acetic, propionic, butyric and lactic acids[2]. The absence of SCFAs has been associated to inflammatory disease (colitis, diarrhoeas) while the presence plays an important role in the protection against colon carcinogenesis[3]. In particular, Butyrate has been recognized for its potential to act on secondary chemoprevention by slowing down grown and activating apoptosis in colon cancer cells.

The aim of this study was to analyze main SCFAs (Butyric, Propionic and Valeric Acid) from vitro and vivo samples by HPLC/DAD and GC/MS.

The GC/MS analysis in literature before determination required a lot of steps as evaporation and derivatization but these acids can be lost in these steps[4,5,6,7]. We analyzed SCFAs in GC/MS without derivatization because we used the Headspace extraction. Samples were weigh in vials and put in incubator at 75°C for 30 minutes. Then 1ml of the head air was inject in GC with program temperature mode and analyzed in MS with Scan mode. The analytic column is a capillary Zebron ZB-624.

The HPLC analysis, instead, requires clean-up process with liquid extraction and Solid Phase Extraction for culture fermentation and real fecal samples.

Analytic column used in HPLC is able to separate short chain organic acid. The Mobil Fase was composed from water content 0.1% of Acetic Acid and Acetonitrile. The maximum wavelength was 205nm.

Real samples were analyzed in HS-GC/MS and HPLC/DAD and we note that some bacterial species production more SCFAs of other.

These analytical methods could be useful for future applications in the diagnosis of several intestinal diseases

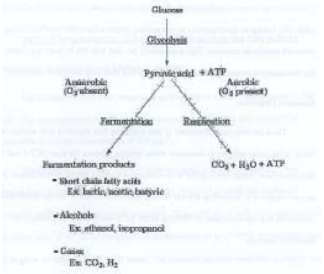

Figure 1: Diagram of the production SCFA

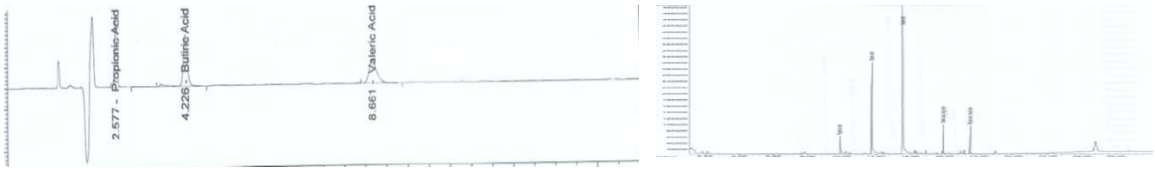

Figure 2: Chromatogram HPLC and GC of standard

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PRECISION OF INTERNAL STANDARD AND EXTERNAL STANDARD METHODS IN HIGH - PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

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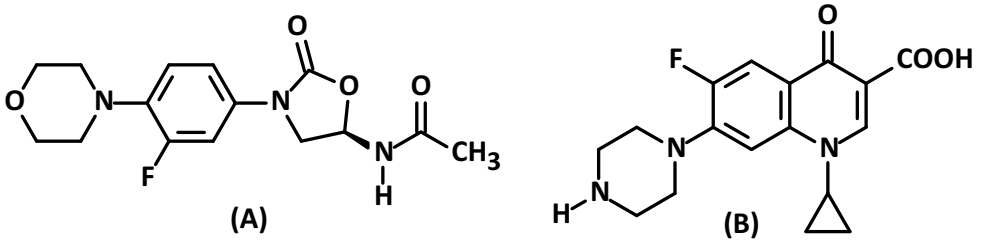
Internal standard methods are used to improve the precision and accuracy of results where volume errors are difficult to predict and control. A systematic approach has been used to compare internal and external standard methods in high performance liquid chromatography (HPLC). The precision was determined at several different injection volumes for HPLC and ultra-high pressure liquid chromatography (UHPLC), with two analyte and internal standard combinations. Precision using three methods of adding the internal standard to the analyte before final dilution was examined. The internal standard method outperformed external standard methods in all instances.

Asystematic approach was used to compare internal standard (IS) and external standard (ESTD) methods used in high performance liquid chromatography (HPLC). The experiments described were specifically designed to examine the precision of the IS method as compared to the ESTD method using the last two generations of HPLC and ultrahigh-pressure liquid chromatography (UHPLC) systems[1].



Two methods of introducing the IS were compared; these methods involved either weighing the amount of IS added as a solid or an internal standard solution of known concentration. Along with two types of instruments, HPLC and UHPLC, we used two analytes, Linezolid (A) and Ciprofloxacin (B), at different concentrations and injection volumes.

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MEPS-UHPLC-PDA METHOD DEVELOPMENT AND VALIDATION FOR THE DETERMINATION OF LINEZOLID AND CIPROFLOXACIN IN HUMAN PLASMA OF HOSPITAL-ACQUIRED PNEUMONIA PATIENTS

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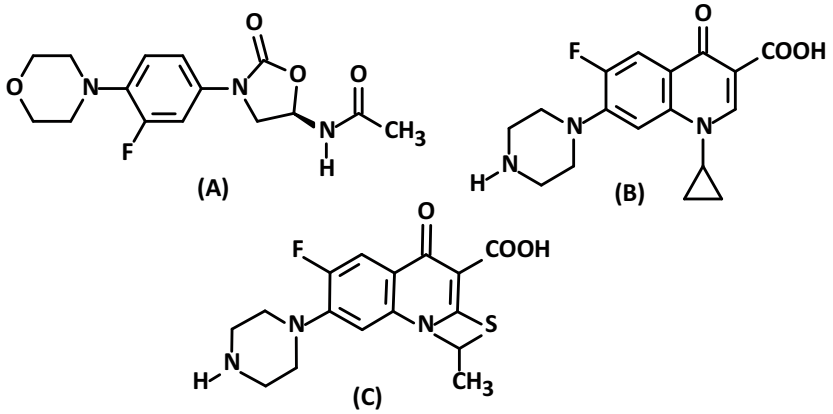
This paper describes the development and the complete validation of an analytical method for the simultaneous determination of linezolid (A) and ciprofloxacin (B), two antibodies used in combination for the initial treatment of Hospital-Acquired Pneumonia (HAP) patients[1], aimed to be used for their therapeutic drug monitoring.

In order to achieve an ultra-fast, sensitive and accurate method but also more environmental-friendly, microextraction by packed sorbent (MEPS)[2] was used as the sample preparation technique combined with ultra-high performance liquid chromatography (UHPLC).



MEPS extraction was optimised and fine-tuned in order to max out efficiency with small sample volumes and in a short time period (3 min. for the entire sample preparation step), using a C_{18} BIN. Chromatography was carried out using a Waters BEH C_{18} (50 x 2.1 mm ID, 1.7µm) column and a gradient elution using ammonium acetate buffer (eluent A) and a mixture of acetonitrile-methanol. Ulifloxacin(C) was chosen as the internal standard.

The method showed good linearity (r^2>0.9994) and high precision (RSD%<6%) for both analytes, as well as high accuracy (96.4 for linezolid, 97.6% for ciprofloxacin). On the analytical method validation basis, the method fulfilled all the requirements according to the International Guidelines[3], showing its suitability for the routine analysis of plasma samples from HAP patients in treatment with linezolid and ciprofloxacin.

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Monitoraggio e Analisi di BVOCs nel Parco dei Monti dei Sibillini

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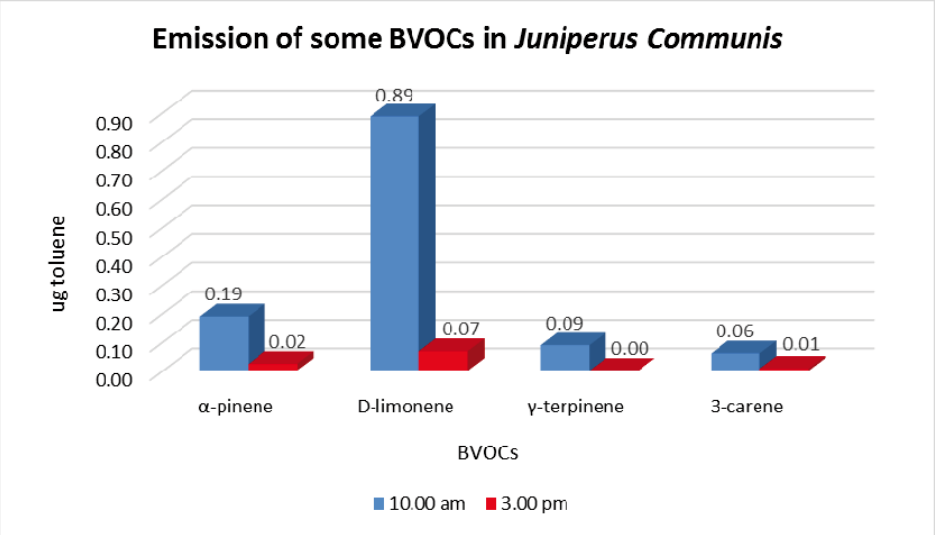
I composti organici biogenici volatili (BVOCs) includono un largo spettro di idrocarburi atmosferici, emessi da sorgenti naturali. I terpenoidi, un ampio gruppo di BVOCs, è costituito da emiterpeni, monoterpeni e sesquiterpeni. L'obiettivo del nostro progetto è monitorare l'emissione dei BVOCs di alcune specie di piante, in particolare, *Juniperus Communis*, *Juniperus Oxycedrus* e *Fagus Sylvatica* presenti nel Parco Nazionale dei Monti Sibillini. Il campionamento è stato effettuato *in situ* con delle fiale adsorbenti (Carbotrap 300) con un flusso di 200 ml/min in orari diversi della giornata, per una volta al mese da Aprile ad Agosto; successivamente le fiale sono state analizzate in laboratorio utilizzando il Desorbitore Termico-GC-MS e la SPME-GC-MS.

Dai risultati ottenuti, abbiamo osservato variazioni interessanti per quello che riguarda le emissioni dei BVOCs più abbondanti.



Uno degli esempi più suggestivi è dato dall'emissione di α-pinene, D-limonene, γ-terpinene e 3-carene dallo Juniperus Communis alle ore 10.00 e 15.00 nel mese di Luglio. Abbiamo notato che queste discrepanze sono dovute a fattori climatici come, ad esempio, umidità, temperatura e periodo dell'anno in cui sono stati effettuati i campionamenti.

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Analysis of pesticides in saffron: clean-up by Solid Phase Extraction using molecularly imprinted polymers

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This work describes the development and application of Molecularly Imprinted Polymers (MIPs) for clean-up of matrix effects in the analysis of herbicides in saffron. Whit this purpose, MIP-based solid-phase extraction is coupled to high-performance liquid chromatography analysis with diode-array detection. MIPs represent a useful alternative to commercially available solid-phase-extraction cartridges for sample clean-up and selective pre-concentration of analytes in complex matrices.[1-3] Crocins, the mono- and di-glycosyl esters of crocetin, are water-soluble carotenoids responsible for the colouring power of saffron. We have synthetized a MIP using as template the mixture of crocins naturally occurring in the spice (croc-MIP). To increase the concentration of the template molecules, a saffron ethanolic extract was preliminarily purified by crystallisation. HPLC was used to evaluate the extraction efficiency and selectivity of croc-MIP and, for comparison, of a polymer imprinted with D-gentiobiose (gent-MIP), a non-imprinted polymer (NIP) and two common commercial cartridges packed with polymeric or C18 stationary phases. SPE based on croc-MIP was applied to saffron samples with the aim of reducing the interference due to the crocins in the analysis of selected triazine herbicides.

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Experimental design combined with response surface technique for the optimization of ion chromatographic system

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The ion chromatography involves several mechanisms for ion separations, such as ion-pairing and ion-exclusion, the majority of the methods are based on chromatographic apparatus equipped with cation or anion exchange stationary phases and conductivity detection.[1,2] The process of ion exchange requires the establishment of electrostatic interactions between the analyte ion and the functional groups of the resin.[3] Statistical design of experiments (DOE) is seen as an important instrument of chemometrics. DOE is able to guarantee that the dependencies between experimental conditions and the effect of the experiments can be estimated reliably with a minimal number of experiments.[4-6] In this work DOE combined with response surface methodology was applied to study the effect of the eluent composition on the retention of common cations in ion chromatography. In particular, we modelled the retention factors of Na^+, K^+, NH_4^+, Ca^{++} and Mg^{++} and the global resolution. Response surfaces were assessed to evaluate interactive effects of percentage of acetonitrile, nitric acid and pyridine-2,6-dicarboxylic acid in the eluent on the above parameters. Nitric acid concentration and acetonitrile content appeared as the most and the least influent components of the eluent in determining the retention factors of individual ions or the global resolution of the chromatogram, while the concentration of the complexing agent exhibits an intermediate role. Acidification of the mobile phase produces a decrease of the retention factors and a progressive deteriorating of resolution, but this effect can be modulated by the concentration of the complexing agent. The proposed method seems suitable to explore the retention phenomena in ion chromatography under application of complex eluent phases.

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DETERMINATION OF CANNABINOIDS AND METABOLITES IN HAIR BY PRESSURIZED LIQUID EXTRACTION AND UHPLC-HRMS

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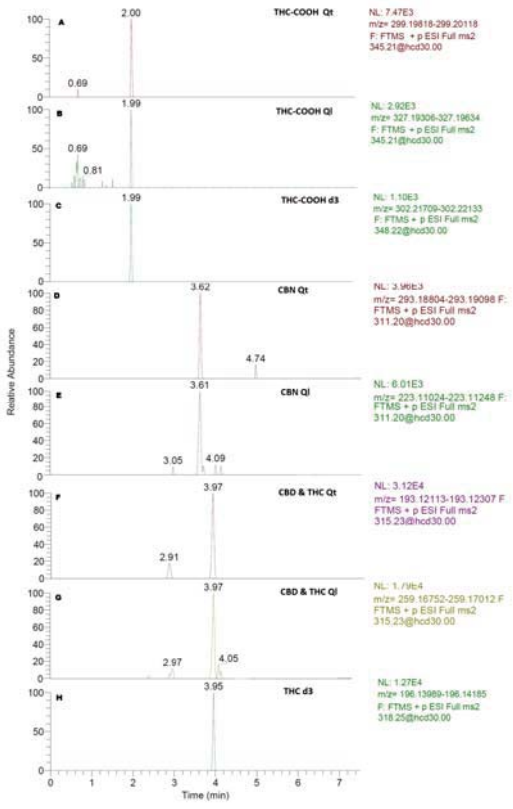
Hair analysis has become a routine procedure in most forensic laboratories since this alternative matrix presents clear advantages over classical matrices; particularly wider time window, non-invasive sampling and good stability of the analytes over time[1]. There are, however, some major challenges for the analysis of cannabinoids in hair, mainly related to the low concentrations of 11-nor-9-carboxy-Δ9-tetrahydrocannabinol (THC-COOH), that is the major metabolite[2]. The determination of THC-COOH has been shown to be crucial to distinguish between passive drug exposure and active consumption since this molecule is an exclusive product of metabolism and can be considered as marker of drug abuse. Other cannabinoids, i.e. cannabinol (CBN) and cannabidiol (CBD) are often quantified as well, since it has been reported that the sum of the major cannabinoids may provide a better indication of drug use than THC alone. The most used approach for sample preparation is based on digestion in alkaline medium using NaOH followed by liquid/liquid extraction (LLE), solid phase extraction (SPE), solid phase micro extraction (SPME) or solid phase dynamic extraction (SPDE). Enzymatic digestion and direct methanol extraction have been also reported but require longer times, up to 5 hours. A drawback of NaOH digestion is that the stability of the analytes might be affected during the digestion procedure, for example CBD is not stable under the severe conditions of alkaline digestion; furthermore large volume of organic solvents are used for LLE procedure and the reproducibility is poor. In this study a fast, accurate and sensitive method for the determination of cannabinol, cannabidiol, THC and THC-COOH in hair has been developed. The extraction of analytes from hair (50 mg) is based on an automated pressurized liquid extraction(PLE) using water modified with the surfactant sodium dodecyl sulphate as eluent phase. PLE extract isthen cleaned up by SPE using polymeric reversed phase cartridges Strata XL before the injection in the HPLC–HRMS/MS system. The Q-exactive high resolution mass spectrometer was crucial in order to have the maximum sensitivity from the analysis of THC-COOH at lowest point. Chromatographic conditions obtained with a fused-core column allowed a good separation of the analytes in less than 4 min. The whole procedure has been validated according to SWG-TOX guidelines.The LLOQs obtained for THC-COOH and the other



analytes were respectively 0.1 and 2 pg/mg. To the best of our knowledge, this is the first LC–MS/MS based method that allows the detection of THC-COOH in hair at values lower than the cut-off.

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DETERMINATION OF HERBICIDES IN BABY FOOD BY MEANS OF MEPS EXTRACTION FOLLOWED BY UHPLC-MS/MS ANALYSIS

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Commission Directive 2006/125/EC sets the rules on the composition and labeling of processed cereal-based foods for particular nutritional use for infants and young children. It also requires that processed cereal-based food and baby food must not contain residues of individual pesticides at levels exceeding 0.003 mg/kg for disulfoton, terbufos, fensulfothion and their metabolites, haloxyfop and its esters, 0.004 mg/kg for fipronil and fipronil-desulfinyl.

The goal of this study was to develop an extraction and purification protocol from baby food matrices, based on rice and cereals, designed for the UHPLC-MS/MS analysis taking into account both recovery efficiency and matrix effect. For this purpose Micro extraction with packed sorbent (MEPS) were used and different sorbent phases were tested; this technology allows to obtain good level of miniaturization and a very small quantities of stationary phase (1-2mg).

The whole procedure is very fast and effective: sample was added with extracting solution (60% of acetonitrile and acetate buffer 10mM pH=5) then the mixture was then sonicated for 5 minutes, and then placed in a water bath at the temperature of 40°C for 5 minutes under constant stirring speed.

The clean-up was carried out with MEPS syringes and the BIN (barrel insert and needle) activation was conducted by taking 100 µL of methanol for three times. The conditioning step was carried out with a solution of water and acetonitrile 90:10 (v:v) for two times. Samples were loaded in extract-discart mode: each aliquot is discarded after passing through the MEPS syringe aspirating aliquots of 250 µL. The 200 µL of eluate were collected in a vial and placed in the autosampler for the subsequent UHPLC-MS/MS analysis.

The chromatographic separation was conducted using a XB-C18 column, 100x2.1 mm, packed with core-shell particles of 1.7 µm. For the identification and quantification of the analytes an UHPLC-MS/MS equipped with a V-source operating in positive ionization (PI) and negative (NI) was used for all analytes. The mobile phases were: water (phase A) and Acetonitrile both 5 mM HCOOH; a linear gradient gradient was applied for the separation, with a total run time of 6.3 minutes. The quantitative analysis was conducted in Multi-Reaction-Monitoring (MRM), selecting two precursor ion/ion transitions for each analyte.

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ANALYSIS OF ADDUCTS OF ACTIVATED PAHS WITH DNA BY MEANS OF MALDI-TOF/MS

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Polycyclic aromatic hydrocarbons (PAHs) are a group of structurally related chemicals produced during a variety of combustion processes [1] and characterized by unusual chemical stability. These ubiquitous environmental pollutants constitute an important class of carcinogenic compounds [2–5] because they can bioaccumulate and then their electrophilic derivatives (i.e. dihydrodiol epoxide metabolites) have been proved to interact with DNA by covalent bonding with the bases adenosine (Ado) and guanosine (Guo). Covalent modification of DNA by a chemical has been demonstrated to be the initial step in chemical carcinogenesis. The presence of adducts can thus be an useful biomarker both in cancer risk assessment [6] and monitoring of environmental and occupational exposure to chemical hazards [7].
Recently, different studies have been conducted also on the toxicity of PAHs exposed to UV and visible light: the photodegradation products have been demonstrated to be mutagenic and to induce DNA damage [8]. This has been hypothesized to occur indirectly, via reactive oxygen species (ROS), or directly, via formation of adducts between some of the photooxidized products of PAHs and DNA.
Detection of DNA adducts is, however, a rather complex matter, because of the low frequency of DNA adduction that occurs in vivo; in fact, techniques that can detect down to 10 pg adducts on 1 mg DNA are required. Mass spectrometric (MS) detection can be an useful tool for the identification of these adducts [9]: most of these studies have been carried out using benzo[a]pyrene (B[a]P) and its derivatives, as model compounds; in fact, B[a]P is known to be the most widespread and probably the most carcinogenic compound among the PAH. In particular, LC–MS–MS has been proved to address sensitivity and specificity issues in the analysis of DNA adducts [10].
In this work, a procedure for detection of activated PAH–oligonucleotide adducts using MALDI-TOF/MS is reported. In the first part of the work, a procedure for detection of the adducts was developed using B[a]P-dihydrodiol epoxide (B[a]PDE) as model compound. B[a]PDE is the major metabolite of B[a]P and its ability to bind DNA is well known. The structures of adducts of B[a]PDE with guanosine and adenosine have been identified and characterized, as well as the adducts with oligonucleotides (GGGG and CCCC).
The developed MALDI-TOF/MS procedure enables rapid, sensitive, and selective analysis of B[a]PDE–nucleosides making possible their detection directly in the reaction mixture without isolation of the adducts and with minimum clean-up. Moreover, it can be potentially applied to any compound forming adducts with nucleosides. In order to prove this concept the second part of the work was devoted to identification and characterization of photodegradation products of B[a]P and to detection of the formation of stable adducts with oligonucleotides under the experimental conditions.
For this purpose different MALDI matrices were tested in order to achieve best sensitivity and specificity due to effective ionization and less interfering peaks: 2',4',6'-Trihydroxyacetophenone monohydrate (THAP) was chosen for its ability to promote oligonucleotide ionization. It was dissolved in a water/acetonitrile solution (75/25 or 50/50) added with formic acid 0.1%.

Photooxidation was carried out using a low-pressure (LP) Hg vapour UV lamp placing 100-µL aliquot of 500 ppm B[a]P in acetonitrile, irradiated for 24 h (1 max 365 nm) at room temperature.
The use of this powerful technique enables adduct detection without previous isolation of the analytes in complex mixtures, as was apparent from the minimal clean-up carried out on the synthesized adducts. Therefore MALDI-TOF/MS seems to have significant potential for detection and characterization of DNA adducts formed with compounds different from PAHs.
The results reported here represent a further evidence of the ability of some photoactivated compounds to bind DNA, pointing out their genotoxicity.

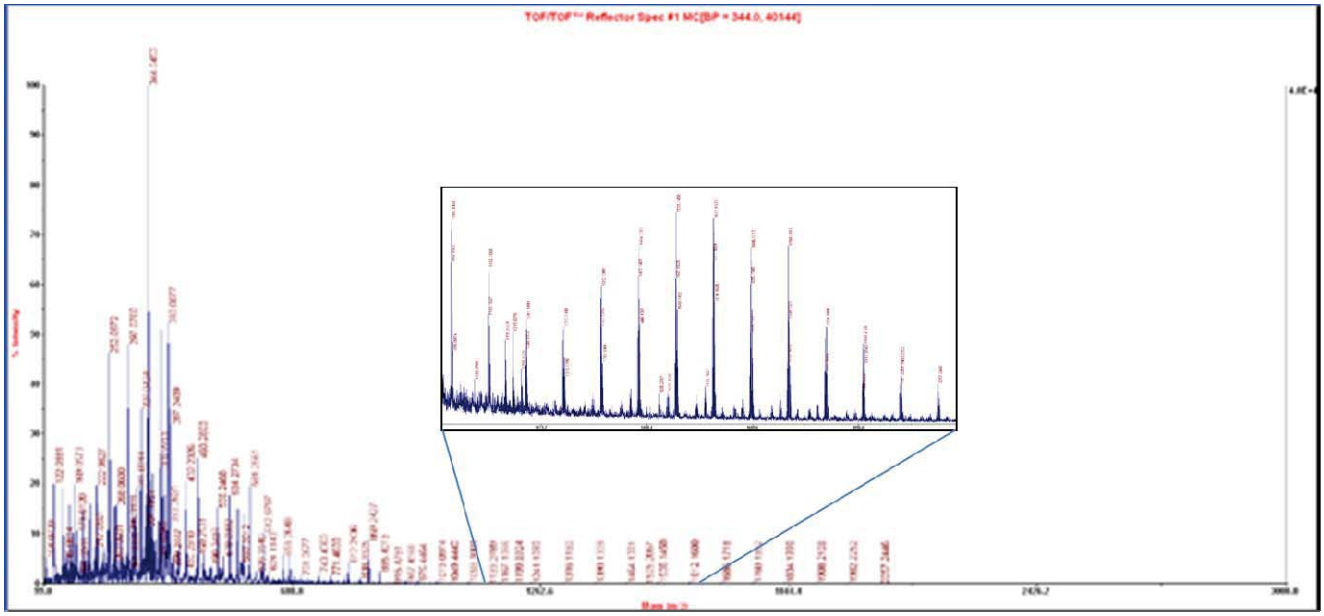

Figure 1: *MALDI-TOF spectrum of a mixture containing GGGG and activated BaP with some adducts highlighted in the zoomed box.*

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DETERMINATION OF FREE FATTY ACIDS IN DAIRY PRODUCTS BY MSPD EXTRACTION FOLLOWED UHPLC-MS/MS ANALYSIS

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In milk and its derivate products the short-chain fatty acids are bonded as triglycerides while only a small fraction is present as free fatty acids (FFAs) in nature, particularly in foods processed with the aid of microorganisms, in which they are aroma substances. [1]. The development of automatic milking systems (AMS) in many larger farms increases the need for quantification of FFAs [2]. Air intake in the AMS system raises the level of FFAs significantly and the mechanical treatment and elevated temperatures result in higher levels of FFAs, due to higher lipolysis [3]. Another factor that affects the level of FFAs in milk is the microbial lipases, which are produced by psychotrophic bacteria [4].

An important functional group is composed by conjungates isomers, in particular the conjugates isomers of linoleic acid ("Conjugated Linoleic Acids, CLA"), a mix of geometric isomers of linoleic acid that are synthesized by the microorganisms of the rumen through the hydrogenation of unsaturated fatty acids and are consequently found in milk and meat. In food there are numerous CLAs isomers that differ in the position of the conjugated double bonds and in geometric orientation; in milk the total content is within 2-30 g/kg of fat [1]. CLAs have important biological activities such as anticarcinogenic and antiatherogenic effects, as demonstrated in animal models.

The most analytical methods for determination of free fatty acids in milk involve complex sample pretreatment that frequently consists of a liquid-liquid extraction using different organic solvent systems [5] either a Solid Phase Extraction (SPE) [6] or a Solid Phase Micro Extraction (SPME) [7]; the analysis of the extracted FFAs often consist in a gas chromatography run that often needs a derivatization step [8]. Most of these methods suffer from their inability to recover all FFAs [8] so there is a need for a sensitive and selective method for an accurate quantification analysis of milk FFAs, especially short chain free fatty acids.

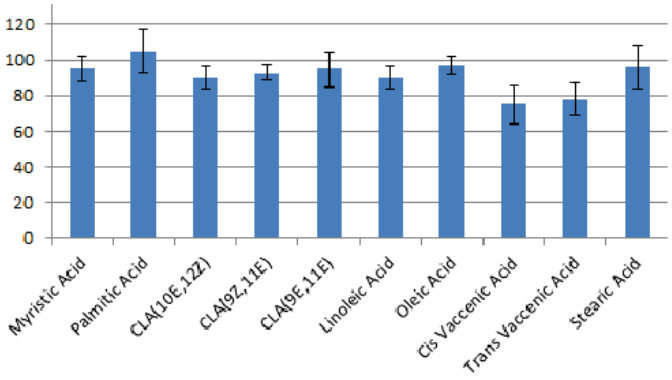

Figure 1: MSPD exctraction recoveries

The present research shows a simple and fast method to identify and quantify the FFAs amount in dairy products through a Matrix Solid Phase Dispersion extraction followed by UHPLC-MS/MS analysis that allows to a rapid pretreatment of the matrix and a short instrumental analysis. FFAs standard solutions and cheese samples were used to validate the proposed method; correlation coefficients of >0.999 were obtained for all of the standards. Recoveries of FFAs were in the range between 75-105%.

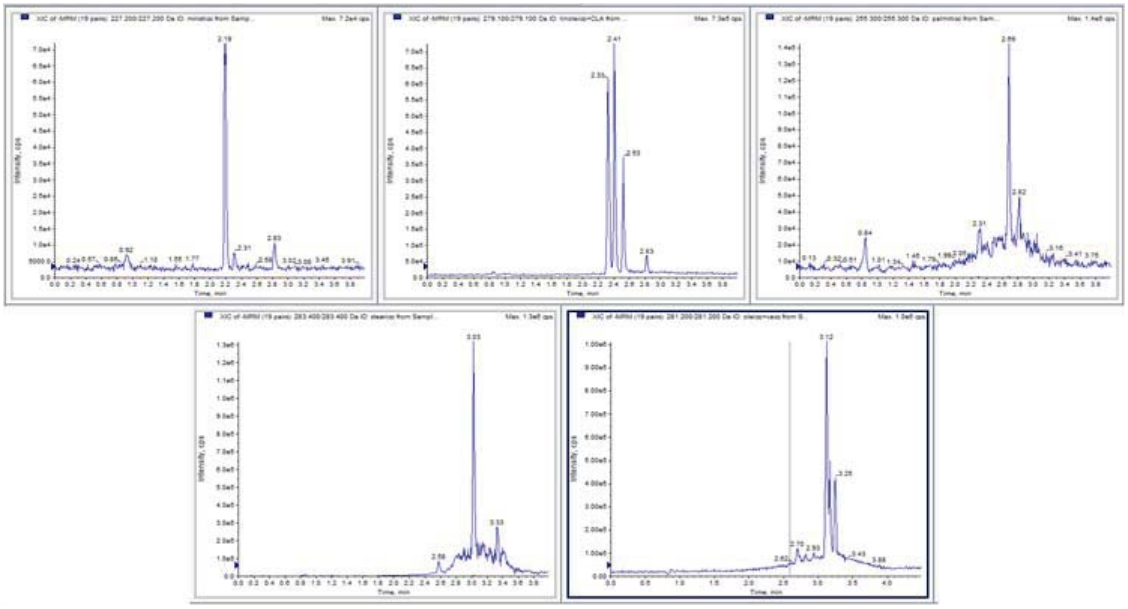

Figure 2: Extracting Ion Currents of Free Fatty Acids

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MULTI-CLASS ANALYSIS OF NEW PSYCHOACTIVE SUBSTANCES IN HAIR BY HPLC-HRMS

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Drug abuse is today a growing global problem that affects every society and people of all ages. Often the consumers are not aware about the type of substances they are using and the correlated risks. In recent years, new psychoactive substances (NPS) often sold as "legal-highs" [1] (psychoactive compounds not included in the list of controlled substances) appeared in the illicit market. These substances are new molecules, natural or synthetic, which are sold in smart shops as incense, bath salts or standard not for human use. The presence of NPS, such as synthetic cathinones, cannabinoids and phenethylamines, which are known to be pharmacologically and toxicologically hazardous, has been frequently reported. More than 500 new psychoactive substances (NPS) have been notified in EU since 2005. The report 2016 of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), reveals that the number of new substances has not declined in the past year with 100 new substances reported for the first time in 2015 [2]. The identification of these new drugs is a never-ending challenge for forensic toxicologists. Screening of drugs of abuse in biological matrices has been traditionally performed with immunological methods that allow rapid and cheap analysis. However, these methods may not be appropriate for the detection of the new molecules continuously appearing on the illicit market [3]. Alternative screening methods are based on chromatography coupled with mass spectrometry (MS); these techniques are the most used in forensic medicine and toxicology for confirmation purposes [4].

The aim of this study was the development of a liquid chromatography–high-resolution mass spectrometry (LC-HRMS) method for a broad screening of NPS in plasma. Data acquisition was in MS/MS and full-scan modes and the method was validated for 25 NPS belonging to different chemical classes (Training Set). Quantitative results have been obtained for these analytes with limits of quantification ranging from 0.03 to 0.4 ng/mL.

The method was proven to be suitable for a wide screening of additional substances, included an in-house database containing over 300 NPS and known metabolites. To this aim, a post-run library matching was conducted for every sample with the library, which may be constantly expanded with new drugs, in order to obtain an effective screening of NPS in biological matrices.

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PHENOLIC ACIDS IDENTIFICATION IN VEGETAL MATRICES: MSPD EXTRACTION AND UHPLC-MS/MS CHARACTERIZATION

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Vegetal matrices contain a wide range of phenolic derivatives including simple phenols, phenolic acids (both benzoic and cinnamic acid derivatives), coumarins, flavonoids, stilbenes, hydrolysable and condensed tannins, lignans and lignins. In plant, phenolics may act as phytoalexins, antifeedants, attractants for pollinators, contributors to the plant pigmentation, antioxidants, and protective agents against UV light, among others [1]. Beside the well-known antioxidant activity, phenolic compounds have received particular attention by the scientific community because of the association with a decreased risk of cardiovascular diseases, cancer and chronic inflammation [2].

Different methods have been developed for separation and determination of polyphenolic compounds; most of them are based on high performance liquid chromatography (HPLC) with UV-Vis detection. However, UV-VIS spectrum does not provide identification of the compounds with the same accuracy of a mass spectrometric approach. Despite the wide range of possible detection modes, the resulting phenolic pattern is extremely dependent by the extraction procedure used. Commonly, the recovery of phenolic acids is carried out with sequential liquid-liquid extractions followed by long purification procedures requiring specific equipment, materials and large amounts of organic solvents. More recently, a valid extraction alternative method is represented by Matrix Solid-Phase Dispersion (MSPD), that requires small quantities of matrix samples and solvents, and can be performed more rapidly [3].

The aim of this work was to optimize a reliable MSPD extraction procedure of PCs contained in common vegetal matrices. Investigations were previously conducted on model systems and after transferred on the freeze-dried basil leaves like real vegetal sample. Different Bondesil Bulk Sorbent (C18 T, HFC18, C18-E, Phenyl, C8, C2) and different washing and elution solutions were tested in order to obtain the best recoveries together with low matrix effect.

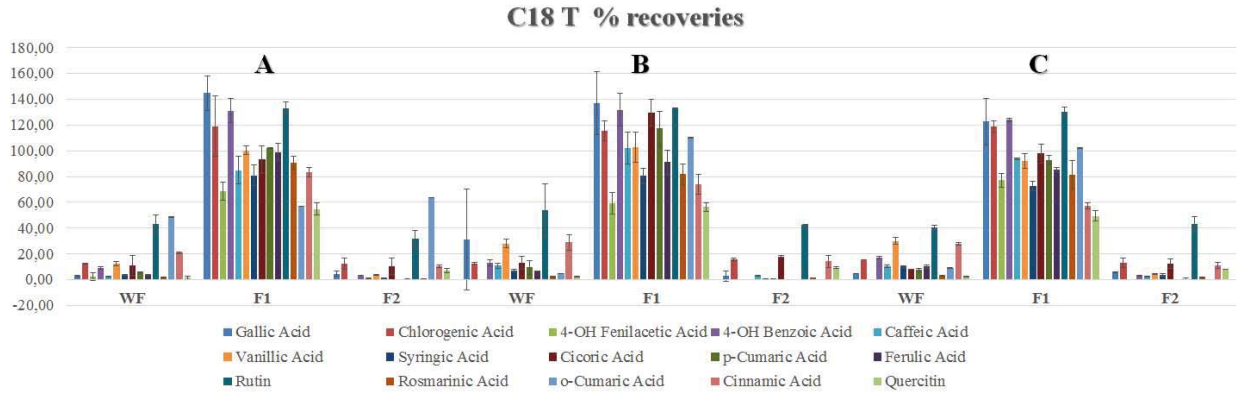

Figure 1: *Recoveries (%) calculated for different Water/Methanol washing solution systems (A) 90:10, (B) 75:25, (C) 60:40. The best results were obtained for System A. (WF – Wash Fraction, F1– First Elution, F2 – Second Elution)*

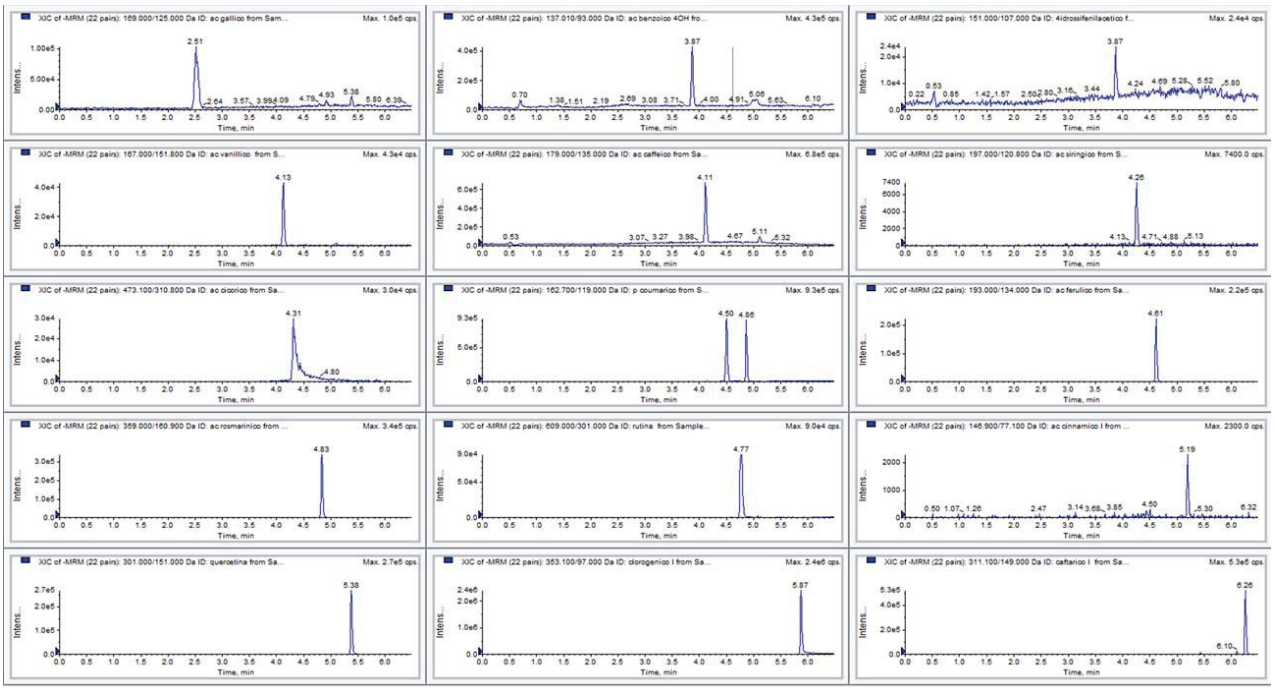

Figure 2: *Extracted Ion Current of the selected analytes*

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UHPLC-PDA ANALYSIS OF FIVE ANTIBIOTICS IN HUMAN PLASMA USING AIR-ASSISTED DISPERSIVE LIQUID-LIQUID MICROEXTRACTION WITH SOLIDIFICATION OF THE FLOATING ORGANIC DROPLET (AA-DLLME-SFO)

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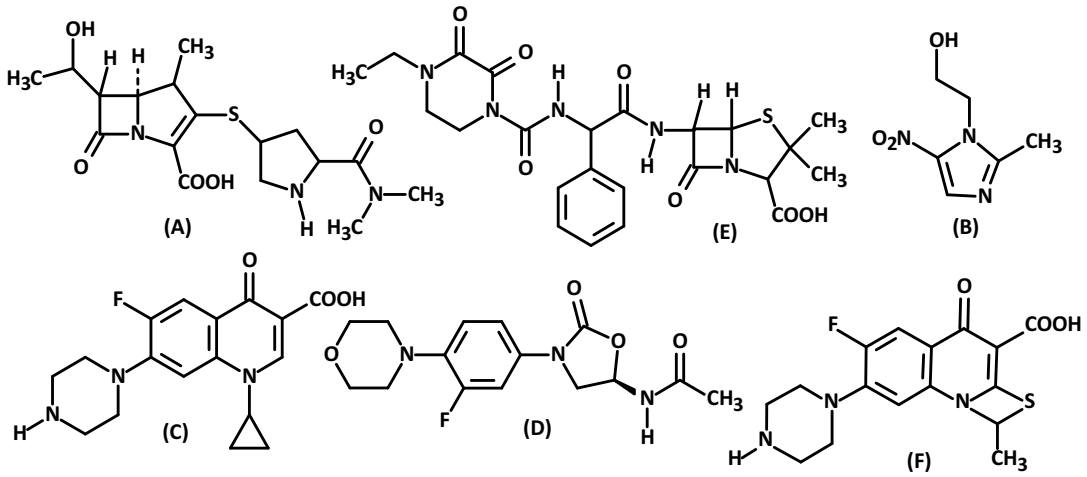
The increase in the incidence of drug-resistant *Gram-positive* pathogens (*e.g. Staphylococcus aureus*) or *Gram-negative (e.g. P. aeruginosa)* has created a great challenge in the treatment of patients with serious infections[1]. To prevent the multidrug resistance an antimicrobial combination therapy may be used.. Recent trends in sample preparation are clearly towards miniaturization, automation, high-throughput performance, on-line coupling with analytical instruments and cost-effectiveness through extremely low or no solvent consumption.



A new microextraction method was developed using extracting solvents which have density lighter than water integrated with the solidification of the organic floating drop (DLLME - SFO)[2]. The extractant solvent may have some requirements : Immiscibility with water, low density, low toxicity and a melting point around room temperature. In the present work, two sample preparation techniques (PP and AA-DLLME-SFO) were combined for the determination of meropenem (A), metronidazole (B), ciprofloxacin(C), linezolid (D) and piperacillin (E) in human plasma by UHPLC-PDA. This combination not only resulted in a high enrichment factor but also offered numerous advantages such as simplicity, ease of operation, low detection limits, short analysis time using extraction solvent with lower toxicity instead of highly toxic solvents.

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QUICK EASY CHEAP EFFECTIVE RUGGED AND SAFE HPLC-PDA METHOD FOR THE SIMULTANEOUS DETERMINATION OF SEVERAL NON STEROIDAL ANTI-INFLAMMATORY DRUGS IN HUMAN PLASMA

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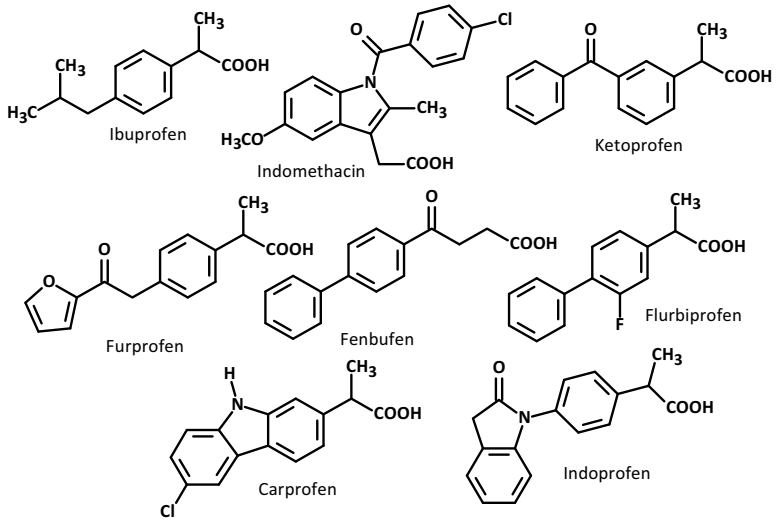
Non steroidal anti-inflammatory drugs (NSAIDs) are the most commonly prescribed drugs for treatment of a variety of pain-related disease, as well as arthritis and other rheumatic disorders, and are incorporated in many cold and allergy preparations; this has caused an increased consumption of NSAIDs. In this scenario the demand of sensitive and selective procedures for the simultaneous analysis of these compounds, both in environmental and biological samples, has increased.



NSAIDs drugs have been extracted by QuEChERS method. This method includes the use of relatively large amounts of inorganic salts in order to allow easy isolation of organic extract phase. The procedure consists in two principal steps: addition of salts to a small amount of plasma and the addition of a small quantity of sorbent material[2].The extract was been quantified using HPLC-PDA. The QuEChERS method can provide a rapid, effective, user-friendly and cheap method for the simultaneous extraction of a wide range of drugs and metabolites, including NSAIDs, and it allows to have the cleanest extracts compared to other sample preparation techniques.

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