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Alessia Ciogli
Curriculum Vitae

Place Roma
Date December, 10th,2018

Part I – General Information

Full Name	Alessia Ciogli
Date of Birth	
Place of Birth	
Citizenship	Italian
Permanent Address	
Mobile Phone Number	
E-mail	
Spoken Languages	Italian, English, French

Part II – Education

Type	**Year**	**Institution**	**Notes (Degree, Experience, …)**
University graduation	2001	Sapienza Università di Roma	Laurea (Master Degree) in Pharmaceutical Chemistry and Technology, 106/110
Post-graduates studies	2006	Sapienza Università di Roma	PhD in Pharmaceutical Sciences (Dottorato di ricerca in Scienze Farmaceutiche, XVIII Ciclo)
Licensure	2002	Sapienza Università di Roma	Qualification as Pharmacist

Part III – Appointments

IIIA – Academic Appointments

Start	**End**	**Institution**	**Position**
1/11/2010	to present	Sapienza Università di Roma	Researcher (Ricercatore Universitario)

Call 2016 (25-07-2017)	2023	Ministero dell'Istruzione dell'Università e della Ricerca (MIUR)	National Scientific Qualification (ASN) as associate professor (Professore di II fascia, Settore Concorsuale 03/C1 – Chimica Organica, SSD CHIM/06). Giudizio di idoneità in **ALL_D-ASN-Giudizi.pdf**
2006	2010	Sapienza Università di Roma	Postdoctoral Fellow. Reaserch activity: Stereoselective separations and applications in pharmaceutical fields (n. 2 Assegni di ricerca biennali)

IIIB – Other Academic Appointments

Start	End	Institution	Position
2015	to present	Sapienza Università di Roma	Member of the training committee for the degree course in Applied Pharmaceutical Sciences (commissione tirocino per il corso di Scienze Farmaceutiche Applicate, SFA)
2015	to present	Sapienza Università di Roma	Member of the student career committee for the degree course in Applied Pharmaceutical Sciences (commissione pratiche studenti per il corso di SFA)
2015	to present	Sapienza Università di Roma	Member of library committee at the Dep. of Chemistry and Drug Technology.
2010	to present	Sapienza Università di Roma	Supervisor for master degree theses in "Chimica e Tecnologia Farmaceutiche" (CTF), Supervisor for degree theses in "Scienze Farmaceutiche Applicate"

IIIC – Other Appointments

Start	End	Institution	Position
01-2008	07-2008	Universität Wien-Austria	Visiting Researcher, topic: Molecular recognition and enantiomer separation technologies

Part IV – Teaching experience

Year	Institution	Lecture/Course
2010-today	Sapienza Università di Roma	"Chimica organica e chimica delle sostanze organiche naturali", canale A-L, degree course SFA, 9 CFU
2005-today	Sapienza Università di Roma	"Esercitazioni di Metodi fisici in chimica organica", master degree course CTF

Part V - Society memberships, Awards and Honors

Year	Title
2012 -	Member of the Italian Chemical Society (SCI)
2013	Rosano C. et al, *ABCB1 Structural Models, Molecular Docking, and Synthesis of New Oxadiazolothiazin-3-one Inhibitors* ACS Medicinal Chemistry Letters **2013**, 4, 694–698, (***published with COVER****)*
2014	Kotoni D. et al, *Separation of complex sugar mixtures on a hydrolytically stable bidentate urea-type stationary phase for hydrophilic interaction near ultrahigh performance liquid chromatography* J. Sep. Sci. **2014**, 37, 527–535 (***published with COVER****)*
2017	De Martino M. et al, *3,5-Dinitrobenzoyl-9-amino-9-deoxy-9-epiquinine as Pirkle-Anion Exchange Hybrid-Type Chiral Selector in High-Performance Liquid Chromatography.* Chromatographia, **2017**, 80, 751–762 invited ***in topical collection "Young Investigators in Separation Science"***
2017	L. Prati et al, *Tetrasubstituted Cyclopentadienones as Suitable Enantiopure Ligands with Axial Chirality*. Organic & Biomolecular Chemistry, **2017**, 15, 8720–8728. (***published with COVER****)*
2018	Mazzoccanti G. et al, *Step-wise "bridge-to-bridge" reduction of monoclonal antibodies and light chain detection: Case studies of tenatumomab and trastuzumab.* Sep Science Plus. **2018,** 1, 261–269 (***published with COVER****)*

Part VI – Other Activities

Year	Title
2013 -	Oral presentations at national and international conferences: 1-Oral: HPLC 2015 (Ginevra, 21-25 giugno). Title: On the use of sub-2 µm Whelk-O 1 stationary phase in enantioselective ultra-high performance SFC. 2-Oral: Incontri di Scienza delle Separazioni (Roma, 12 dicembre 2014). Title: Le potenzialità della fase stazionaria chirale sub-2 µm Whelk-O1 in cromatografia supercritica: dal confronto con l'UHPLC enantioselettiva alla risoluzione di un'ampia library di prodotti. 3-Oral: ChirItaly-2014 (Pisa, 18-20 giugno 2014). Title: Separation science and technology: applications to chiral molecules. 4-Lecture at "Attilio Corbella" Summer School on Organic Synthesis XXXVIII Edition (Gargnano, 17-21 giugno 2013). Title: Meso- and Microfluidic techniques.
2004 -	Collaboration with international and national research groups: • Prof. Philip Stephen e Dr. Frank Devlin, University of Southern California (USA) • Prof. Andrea Mazzanti, Università di Bologna, Italy. • Dr. Giorgio Bencivenni, Università di Bologna, Italy. • Prof. Alberto Cavazzini, Università di Ferrara, Italy. • Prof. Paolo Melchiorre, ICIQ Tarragona, Spain.

	• Dr. Fabia Grisi, Università di Salerno, Italy. • Dr. Jelena Kocergin, Regis' Chromatography and Separations business, Regis Technologies Inc. (IL, USA). • Dr. Donatella Capitani, Istituto di Metodologie Chimiche CNR, Area della Ricerca di Roma 1. Monterotondo Roma.
2015-	Reviewer for several scientific international journals: J. Chromatography A, J. of pharmaceutical and biomedical analysis, J. Separation Science, Catalysis, Nature Communications.

Part VII - Funding Information [grants as PI-principal investigator or I-investigator]

Year	Title	Program
2017	Conformational enantiomers of drugs and drug-like molecules: a combined investigation by chromatographic, spectroscopic and computational methods. **(I)**	Sapienza Università di Roma (Ateneo2017)
2017	Fondo per il Finanziamento della Attività Base di Ricerca – FFABR.	MIUR
2016	Preparazione e caratterizzazione di fasi stazionarie contenenti selettori misti, dotati di complementarietà funzionali focalizzate alla ricognizione molecolare e/o alla promozione *on-column* di processi chimici secondari a quello della ripartizione cromatografica. **(I)**	Sapienza Università di Roma (Ateneo2016)
2014	Preparazione, caratterizzazione strutturale e analisi dell'attività espressa da organo-catalizzatori ed enzimi immobilizzati covalentemente su matrici solide mesoporose, utilizzabili per lo sviluppo di efficaci procedure sintetiche in fase eterogenea. (**PI)**	Sapienza Università di Roma (Ateneo2014) Code: C26A143MYA
2009	Progettazione, sintesi e studio di molecole e materiali innovativi con proprietà ottimali di ricognizione molecolare: applicazioni a sistemi di separazione cromatografici ad elevate prestazioni. **(I)**	PRIN 2009, 2011-2014
2006	Processi di solubilizzazione, purificazione e separazione di nanotubi di carbonio. **(I)**	PRIN 2006, 2007-2009
2005	Sistemi di separazione ad elevate prestazioni basati sul riconoscimento molecolare chemo- e stereoselettivo.**(I)**	PRIN 2005, 2006-2008
2004	Sintesi, proprietà e applicazioni di fullereni e nanotubi di carbonio funzionalizzati. **(I)**	PRIN 2004, 2004-2006

Part VIII – Research Activities

The research activity can be arranged in two main lines: i) synthesis of chromatographic supports for molecular recognition studies and ii) study of stability/instability of bioactive compounds mainly enantiomers. The first line focuses in the field of separation science and includes as corollary some studies of advanced methodologies in

the analysis of chiral and bioactive molecules. The second line is related to stereochemistry and it has become the most studied in the last years of my research activity. Overall, both lines are interconnected and originate from an interdisciplinary research program that reflects skills acquired in synthetic organic chemistry, stereochemistry, chemistry of materials and in separation science. An overview of my scientific production is briefly presented with the accent on the results described in the selected publications (**A1-A12**) as requested by the PA upgrade call.

The synthesis of new chromatographic supports has characterized above all the first period of my research activity (2004-2012) although continuing to be present in all my scientific production. Several functional molecules have been linked to solid supports in order to investigate their recognition properties in particular towards molecules of biological and pharmaceutical interest. Functional molecules, grouped according to their size, are low molecular weight enantiopure molecules, receptor-type structures and polymeric materials. These molecules, once immobilized onto high-surface area porous materials, are able to interact at two different levels, broadly or selectively, with several classes of compounds. Silica supported macrocyclic glycopeptides, mainly based on teicoplanin, have been largely investigated because of their resolution ability towards the enantiomers of many chiral compound classes (derivatized and free amino acids, peptides, carboxylic acid, aryl sulfoxides, aliphatic amines). To further extend their applicability, a modified synthetic procedure was designed to obtain chromatographic media with a bimodal surface distribution where the external surface of the pores is functionalized with a biocompatible hydrophilic achiral polymer (ensuring the molecular exclusion of medium to high molecular weight components), while the internal surface is available for chiral receptor anchoring. These materials are particularly useful in pharmacokinetic studies of substances contained in biological matrices (plasma, blood, urine) avoiding multi-step sample preparation procedures. Further studies in the field of bio-applications were directed towards polymeric organic monoliths as supports for either the preparation of enzymatic reactors or for protein analysis (intact and reduced monoclonal antibodies). Studies of molecular recognition were conducted employing selectors designed to interact with vey polar molecules in polar media. Urea-type bidentate selector, disaccharides bonded on silica via click copper-catalyzed azide–alkyne cycloaddition, and aryl or alkyl perfluorinated materials were selected as ideal candidates for hydrophilic interaction chromatography (separation of very polar compounds, such as carbohydrates, amino acids, and flavonoids). In particular, for the fluorinated stationary phases (**A2**), a combination of different techniques (solid-state NMR experiments, low-temperature nitrogen adsorption, elemental analysis and some chromatographic measurements) provided a detailed picture of the structural characteristics and properties of these materials. Alternately, a bromoundecyl resorc[4]arene, in the cone stereoisomeric arrangement, was linked to silica to generate a HPLC stationary phase able to well resolve the E/Z isomers of a series of semisynthetic anticancer combretastatins (**A11**).

One different application of chromatographic methods, far from the goal of separating molecules, is the study of the specific interactions between bonded molecules and a specific target. In this context, the interactions of short peptides with carbon nanotubes (single-walled- and multi-walled-nanotubes, SWNT and MWNT) were investigated using covalently bonded SWNT or MWNT on mesoporous silica particles. In this case, the chromatographic approach was advantageous compared to the study in solution, because the nanotubes are slightly soluble in organic/aqueous solvents. More recently (**A12**), to better define the molecular recognition of silver thiolate towards aromatic compounds, a series of benzene derivatives were used as probes in argentation chromatography. Starting from the retention and selectivity observed on a silver mercaptopropyl stationary

phase, density functional theory (DFT) calculations helped to rationalize the experimental results: benzenes bearing electron withdrawing groups were retained longer than those containing electron donating substituents. In addition, molecules characterized by structural properties compatible with a double contemporary coordination with two mercapto-Ag selector arms are able to interact with sporadic double coordination events, in which the second level of coordination is synergistically increased by the establishment of the first one.

From the technological point of view, in the last years the separations of enantiomers focused on the "speed" factor. The impressive number of chiral and potentially active molecules involves many research fields: from organic synthesis to pharmaceutical analysis and from agrochemistry and food science to bioanalysis. Bearing in mind that discrete amounts of single enantiomer with high degree of purity are needed for the different stages of the research (during drug development as an example), the separation of enantiomers could be, if too slow, a limiting step, time consuming, and costly in the whole productive process. For this reason, typical chromatographic analysis time of 20 min can narrow productivity. Today, analytical methods prefer run times of few minutes or below 60 seconds for separations at high efficiency and resolution. This can be obtained by combining the use of chromatographic supports based on small particles, short columns and suitable instrumentation (with reduced extra-column volume). Starting in 2010, we began to transfer the low-molecular weight chiral selectors (bis-(3,5-dinitrobenzoyl)-derivative of trans-1,2-diaminocyclohexane (DACH-DNB), WhelK-O1, teicoplanin and some derivatives of quinine) on the new generation of silica particles (sub-3micron and sub-2micron particle diameter) allowing faster and higher efficient analysis (**A6**). The interest in this field is confirmed by increased publications, mainly from industrial word, and by some reviews on the state-of-art (**A3**, **A10**).

The second topic of my research activity concerns the study of stereochemical stability of bioactive compounds as potential new drugs or organocatalysts in asymmetric synthesis. In general, the stereochemical stability of enantiomers is of particular interest, because their action is closely related to their absolute configuration and to the stability of the stereogenic elements (centers, axis) present in the structure. Depending on the involved energy barriers separating stereolabile enantiomers, different scenarios can occur: highly stable enantiomers (an energy barrier of 27 kcal/mol corresponds to a half-life of 80 days at 25°C), enantiomers that undergoes enantiomerization at room temperature (or closer), and fast interconverting enantiomers. Using classical kinetic techniques (off-column approach) it is possible to know the energies involved in the racemization processes starting from enantiopure species in solution. The progress of the racemization is monitored by chromatographic or chiro-optical methods. Thus, this approach is useful for highly stable enantiomers. For interconverting enantiomers having energy barriers in the 18-27 kcal/mol energy window, the barrier can be obtained by dynamic chromatography (D-HPLC or on-column approach). During a chromatographic separation process the solutes can be involved in secondary equilibria (reversible isomerizations). If these equilibria occur at the same timescale of the separation process, the elution profile is deformed. In the simplest case of two conformational enantiomers resolved on a chiral stationary phase, a typical plateau area will appear between the peaks of the two solutes. The phenomenon depends on the temperature of the chromatographic column and on the flow of the mobile phase. The simulation of these anomalous chromatographic profiles through the use of an appropriate software provides the value of the energy involved in the isomerization process. Both off-column and on-column techniques are usually conducted at variable temperatures to determine enthalpy and entropy contributions to the enantiomerization-racemization process. For very fast isomerization processes (below 16-17 kcal/mol), the on-column approach has limitations and can be replaced with dynamic NMR (D-NMR). The

ranges of applicability of both NMR and HPLC dynamic techniques are not fixed and often they can be at the same time applied to independently evaluate the same process or to investigate the dynamics of multiple flexible elements of chirality having different stabilities (i.e. two axis or one axis and one center). Focusing on axial chirality, the dynamic techniques help research in organocatalysis providing stable atropoisomeric catalysts (**A9**, **A7**) or studying the mechanisms by which the axial chirality of the products is controlled by the enantiopure organocatalyst (**A1**, **A4**, **A5**). In the first item, the possibility to produce atropisomeric tetrasubstituited cyclopentadienones as organocatalysts was investigated (**A9**). The steric requirement of aryl substituent has been assessed by means of D-HPLC and D-NMR. Among the investigated compounds, the more stable atropisomers (racemization energy >35 kcal/mol at room temperature) have been resolved by enantioselective HPLC and the absolute configuration has been assigned by comparison of DFT and electronic circular dichroism (ECD) computed spectra with experimentally determined ones. The atropisomeric phencyclone derivatives were used in the synthesis of enantiopure Shvo catalysts and employed in enantioselective hydrogenation catalytic reactions. A similar approach (stability of precursor or of catalyst, absolute configuration determination) was adopted in the design of chiral ruthenium catalysts with C1-symmetric N-Heterocyclic carbenes ligands for asymmetric olefin methatesis reactions (**A7**). Alternately, D-HPLC was used in the study of remote control of the axial chirality of atropisomeric succinimides via an aminocatalytic vinylogous Michael addition/desymmetrization sequence of N-arylmaleimides. (**A4**, **A5**). The importance of intramolecular NO2/CO weak interaction (e.g. in 3,4 bisarylmaleimides and similar scaffolds) was investigated to measure the energy of this non covalent interaction that can modulate the conformational preferences and stereoselectivity of some organocatalysts (**A1**). In addition, atropisomerism of rhodanine derivatives, as potential new drugs, (systems bearing 3-aryl-4-hydroxy-thiazolidine-2-thione portion) was observed and N-aryl rotational energy barriers were measured using both dynamic NMR and HPLC techniques. The combined dynamic approach provided some interesting information on stability of this substituted thiazolidinic ring in acid media (**A8**).

Finally, as consequence of interaction or fusion of two research lines, a large part of last two years was dedicated to development of supported organocatalyst for heterogeneous batch and flow catalysis. Silica-based or polymethacrylate-based solid media were prepared to covalently anchor 9-amino-9-deoxy epiquinine as preferred catalyst for asymmetric reactions. Michael additions was realized with good yield and high stereocontrol. First results of last work will be soon published.

Part IX – Summary of Scientific Achievements

The list of all publications is in attachment E (**ALL_E_publications.pdf**).

Product type	Number	Data Base	Start	End
Papers [international]	68*****	Scopus	2004	2018
Chapter Book	4			

*****68 refers solely to scientific journals with impact factor.

Index	Database	Value	Value without self-citations of the author
Total Impact factor *	ISI Journal Citation Report	287.071	
Average Impact Factor per Product	ISI Journal Citation Report	4.222	
Total Citations	Scopus	1236	1116
Average Citations per Product	Scopus	18.176	16.412
Hirsch (H) index	Scopus	20	18

*****Calculated on the basis of the publication year for the 68 papers (22/11/2018).

Part X– Selected Publications (n. 12)

A1) Chiarucci M.; Ciogli A.; Mancinelli M.; Ranieri S.; Mazzanti A. "The Experimental Observation of the Intramolecular NO2/CO Interaction in Solution"
Angew. Chem. Int. Ed., **2014**, 53 (21), 5405 – 5409.
DOI: 10.1002/anie.201402366; **IF = 11.261 – cited 6 time -** SOURCE: Scopus

A2) Ciogli A.; Simone P.; Villani C.; Gasparrini F.; Laganà A.; Capitani D.; Marchetti N.; Pasti L.; Massi A.; Cavazzini A. "Revealing the fine details of functionalized silica surfaces by solid-state NMR and adsorption isotherm measurements: the case of fluorinated stationary phases for liquid chromatography"
Chemistry - A European Journal, **2014**, 20, 8138 – 8148.
DOI: 0.1002/chem.201304330; **IF = 5.731 – cited 3 times -** SOURCE: Scopus

A3) Cavazzini A., Marchetti N., Guzzinati R., Pierini M., Ciogli A., Kotoni D., D'Acquarica I., Villani C., Gasparrini F. "Enantioseparation by ultra-high-performance liquid chromatography"
Trend in Analytical chemistry (TrAC), **2014**, 95 – 103
DOI: 10.1016/j.trac.2014.026; **IF = 6.472 – cited 38 times -** SOURCE: Scopus

A4) Di Iorio N., Righi P., Mazzanti A., Mancinelli M., Ciogli A., Bencivenni G.- "Remote Control of Axial Chirality: Aminocatalytic Desymmetrization of N-Arylmaleimides via Vinylogous Michael Addition."
J. Am. Chem. Soc., **2014**, 136, 10250 − 10253.
DOI: 10.1021/ja505610k; **IF = 12.113 – cited 47 times -** SOURCE: Scopus

A5) Eudier F., Righi P., Mazzanti A., Ciogli A., Bencivenni G.- "Organocatalytic Atroposelective Formal Diels−Alder Desymmetrization of N-Arylmaleimides."
Organic Letters, **2015**, 17(7), 1728 – 1731.
DOI: 10.1021/acs.orglett.5b00509; **IF = 6.732 – cited 20 times -** SOURCE: Scopus

A6) Sciascera L., Ismail O., Ciogli A., Kotoni D., Cavazzini A., Botta L., Szczerba T., Kocergin J., Villani C., Gasparrini F.- "Expanding the potential of chiral chromatography for high-throughput screening of large compound libraries by means of sub–2 µm Whelk-O 1 stationary phase in supercritical fluid conditions."
Journal of Chromatography A, **2015**, 1383, 160 – 168.
DOI: 10.1016/j.chroma.2015.01.042; **IF = 3.926 – cited 35 times -** SOURCE: Scopus

A7) Paradiso V., Menta S., Pierini M., Della Sala G., Ciogli A., Grisi F.– "Enantiopure C1-symmetric N-Heterocyclic Carbene Ligands from Desymmetrized meso-1,2-Diphenylethylenediamine: Application in Ruthenium-Catalyzed Olefin Metathesis."
Catalysts **2016**, 6, 177.
DOI:10.3390/catal6110177; **IF = 3.082 – cited 3 times -** SOURCE: Scopus

A8) Ciogli A., Kumar S. V., Mancinelli M., Mazzanti A., Perumal S., Severi C., Villani C.- "Atropisomerism in 3-arylthiazolidine-2-thiones. A combined dynamic NMR and dynamic HPLC study."
Organic & Biomolecular Chemistry, **2016**, 14, 11137 – 11147.
DOI: 10.1039/C6OB02145J; **IF = 3.559 – cited 5 times -** SOURCE: Scopus

A9) L. Prati, M. Mancinelli, A. Ciogli, Mazzanti A.- "Tetrasubstituted Cyclopentadienones as Suitable Enantiopure Ligands with Axial Chirality."
Organic & Biomolecular Chemistry, **2017**, 15, 8720 – 8728.
DOI: 10.1039/ c7ob01455d; **IF = 3.564 – cited 1 times -** SOURCE: Scopus

A10) Ciogli A., Ismail O.H., Mazzoccanti G., Villani C., Gasparrini F.- "Enantioselective Ultra-High Performance LC and SFC: the race to the shortest chromatogram."
Journal of Separation Science, **2018**; 41(6), 1307 – 1318.
DOI: 10.1002/jssc.201701406; **IF = 2.557 – cited 14 times -** SOURCE: Scopus

A11) Corradi S., Mazzoccanti G., Ghirga F., Quaglio D., Nevola L., Massera C., Ugozzoli F., Giannini G., Ciogli A., D'Acquarica I. Synthesis of Bromoundecyl Resorc[4]arenes and Applications of the Cone Stereoisomer as Selector for Liquid Chromatography
Journal of Organic Chemistry, **2018**, 83, 15, 7683 – 7693.
DOI: 10.1021/acs.joc.8b00488; **IF = 4.849 – cited 0 times -** SOURCE: Scopus

A12) Menta S., Ciogli A., Villani C., Gasparrini F., Pierini M.- "Recognition mechanism of aromatic derivatives resolved by argentation chromatography: The driving role played by substituent groups."
Analitica chimica Acta **2018**, 1019, 135 – 141.
DOI: 10.1016/j.aca.2018.02.038; **IF = 4.950 – cited 0 times -** SOURCE: Scopus

Roma, 10 dicembre 2018

Alessia Ciogli