



## **DR. ROCCALDO SARDELLA – RICERCATORE CHIM/08**

### **Principali Temi di Ricerca:**

Applicazione di strategie d'analisi avanzate per:

1. studiare l'effetto della composizione della fase mobile e delle caratteristiche strutturali della fase stazionaria sul meccanismo di riconoscimento stereoisomerico nei vari domini della cromatografia chirale;
2. implementare metodi separativi e indici cromatografici derivati in grado di facilitare la valutazione di proprietà chimico-fisiche di composti d'interesse farmaceutico;
3. quantificare i livelli di potenziali biomarcatori molecolari di condizioni patologiche, in fluidi e tessuti biologici;
4. quantificare specifici composti bioattivi in matrici alimentari.

### **Coordinamento:**

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### **Collaborazioni extra-dipartimentali:**

- ✓ Prof. Michael Lämmerhofer, Institute of Pharmaceutical Sciences, University of Tübingen, Tübingen, Germany.
- ✓ Prof. Wolfgang Lindner, Department of Analytical Chemistry, University of Vienna, Vienna, Austria.
- ✓ Prof. Erden Banoglu, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Gazi University, Ankara, Turkey.
- ✓ Prof. Oliver Werz, Institute of Pharmacy, Friedrich-Schiller-University Jena, Jena, Germany.

- ✓ Prof. Joaquín María Campos, Departamento de Química Farmacéutica y Orgánica, Facultad de Farmacia, Granada, Spain.
- ✓ Dr. Maria Luisa Ruiz del Castillo, Instituto de Ciencia y Tecnología de Alimentos y Nutrición (ICTAN), Consejo Superior de Investigaciones Científicas (CSIC) Madrid, Spain.
- ✓ Prof.ssa Federica Pellati, Dipartimento di Scienze della Vita, Università degli Studi di Modena e Reggio Emilia, Modena.
- ✓ Dr. Vincenzo Formica, Medical Oncology Unit - Internal Medicine Department "Tor Vergata" University Hospital, Roma.
- ✓ Prof. Roberto Mandrioli, Dipartimento di Scienze per la Qualità della Vita (QuVi), Alma Mater Studiorum, Università di Bologna, sede di Rimini.
- ✓ Prof. Carlo Bertucci, Dipartimento di Farmacia e Biotecnologie (FaBiT), Alma Mater Studiorum, Università di Bologna, Bologna.
- ✓ Prof.ssa Laura Mercolini, Dipartimento di Farmacia e Biotecnologie (FaBiT), Alma Mater Studiorum, Università di Bologna, Bologna.
- ✓ Prof. Beniamino Cenci Goga, Dipartimento di Medicina Veterinaria, Università degli Studi di Perugia, Perugia.
- ✓ Dr. Alessandro Di Michele, Dipartimento di Fisica e Geologia, Università degli Studi di Perugia, Perugia.

#### **Pubblicazioni degli ultimi 5 anni (2009-2013):**

1. B. Natalini, **R. Sardella**, G. Carbone, A. Macchiarulo, A. Gioiello, R. Pellicciari. Derived chromatographic indices as effective tools to study the self-aggregation process of bile acids. *J. Pharm. Biomed. Anal.* *50* (2009) 613.
2. R. Arnell, P. Forssén, T. Fornstedt, **R. Sardella**, M. Lämmerhofer, W. Lindner. Adsorption behavior of a quinidine carbamate based chiral stationary phase: the role of the additive. *J. Chromatogr. A* *1216* (2009) 3480.
3. B. Natalini, **R. Sardella**, G. Carbone, A. Macchiarulo, R. Pellicciari. The effect of the copper(II) salt anion in the Chiral ligand-exchange chromatography of amino acids *Anal. Chim. Acta.* *638* (2009) 225.
4. B. Natalini, **R. Sardella**, A. Gioiello, G. Carbone, M. Dawgul, R. Pellicciari. Side-chain modified bile acids: chromatographic separation of 23-methyl epimers. *J. Sep. Sci.* *32* (2009) 2022.

5. M.C. Fulco, M. Marinozzi, B.E. Çaliskan, **R. Sardella**, B. Natalini, R. Pellicciari. Synthesis and chromatographic enantioresolution of conformationally constrained analogues of homotaurine. *Tetrahedron* 65 (2009) 8756.
6. R. Pellicciari, A. Gioiello, A. Macchiarulo, C. Thomas, E. Rosatelli, B. Natalini, **R. Sardella**, M. Pruzanski, A. Roda, E. Pastorini, K. Schoonjans, J. Auwerx. Discovery of 6a-ethyl-23(*S*)-methyl-cholic acid (S-EMCA, INT-777) as a potent and selective agonist for the TGR5 receptor, a novel target for diabetes. *J. Med. Chem.* 52 (2009) 7958.
7. B. Natalini, **R. Sardella**, N. Giacchè, S. Palmiotto, E. Camaioni, M. Marinozzi, A. Macchiarulo, R. Pellicciari. Chiral ligand-exchange separation and resolution of extremely rigid glutamate analogs: 1-aminospiro[2.2]pentyl-1,4-dicarboxylic acids. *Anal. Bioanal. Chem.* 397 (2010) 1997.
8. B. Natalini, N. Giacchè, **R. Sardella**, F. Ianni, A. Macchiarulo, R. Pellicciari. Computational studies for the elucidation of the enantiomer elution order of amino acids in Chiral Ligand-Exchange Chromatography. *J. Chromatogr. A* 1217 (2010) 7523.
9. B. Natalini, **R. Sardella**, A. Gioiello, E. Rosatelli, F. Ianni, E. Camaioni, R. Pellicciari. Fast chromatographic determination of the bile salt critical micellar concentration. *Anal. Bioanal. Chem.* 401 (2011) 267.
10. B. Natalini, **R. Sardella**, S. Massari, F. Ianni, O. Tabarrini, V. Cecchetti. Synthesis and chromatographic enantioresolution of anti-HIV quinolone derivatives. *Talanta* 85 (2011) 1392.
11. B. Natalini, **R. Sardella**, A. Macchiarulo, M. Marinozzi, E. Camaioni, R. Pellicciari, Mechanistic aspect and applications of chiral ligand-exchange chromatography, in *Advances in Chromatography* (Vol. 49, Cap. 3), Eli Grushka, Nelu Grinberg (Eds.), CRC Press, Taylor & Francis Group, 2011, 71-134.
12. M. Marinozzi, A. Carotti, E. Sansone, A. Macchiarulo, E. Rosatelli, **R. Sardella**, B. Natalini, G. Rizzo, L. Adorini, D. Passeri, F. De Franco, M. Pruzanski, R. Pellicciari. Pyrazole[3,4-*e*][1,4]thiazepin-7-one derivatives as a novel class of Farnesoid X Receptor (FXR) agonists. *Bioorg. Med. Chem.* 20 (2012) 3429.
13. B. Natalini, **R. Sardella**, F. Ianni. Cromatografia Chirale a Scambio di Ligandi: una vecchia tecnica per nuovi studi computazionali. *La Chimica e l'Industria* 3 (2012) 98.
14. B. Natalini, **R. Sardella**. Chromatographic separation and analysis: chiral ion and ligand exchange stationary phases, in *Comprehensive Chirality* (Cap. 8.8), George Tranter (Ed.), Elsevier, 2012, 115-152.

15. **R. Sardella**, A. Macchiarulo, A. Carotti, F. Ianni, M. E. García Rubiño, B. Natalini. Chiral mobile phase in ligand-exchange chromatography of amino acids: Exploring the copper(II) salt anion effect with a computational approach. *J. Chromatogr. A* *1269* (2012) 316.
16. F. Venturoni, A. Gioiello, **R. Sardella**, B. Natalini, R. Pellicciari. Continuous flow synthesis and scale-up of glycine- and taurine-conjugated bile salts. *Org. Biomol. Chem.* *10* (2012) 4109.
17. **R. Sardella**, F. Ianni, B. Natalini, G.P. Blanch, M.L. Ruiz del Castillo. Rapid detection of D-amino acids in cheese with a chiral ligand-exchange chromatography system. *Curr. Anal. Chem.* *8* (2012) 319.
18. **R. Sardella**, F. Ianni, Nicola Giacchè, A. Lisanti, P. Conti, A. Pinto, L. Tamborini, B. Natalini. Ligand-exchange enantioresolution of dihydroisoxazole amino acid derivatives acting as glutamatergic modulators. *Trends Chromatogr.* *7* (2012) 43.
19. A. Gioiello, **R. Sardella**, E. Rosatelli, B.M. Sadeghpour, B. Natalini, R. Pellicciari. Novel stereoselective synthesis and chromatographic evaluation of *E*-guggulsterone. *Steroids* *77* (2012) 250.
20. **R. Sardella**, M. Marinozzi, F. Ianni, A. Lisanti, B. Natalini. Simultaneous diastereo- and enantioseparation of farnesoid X receptor (FXR) agonists with a quinine carbamate-based chiral stationary phase. *Anal. Bioanal. Chem.* *405* (2013) 847.
21. M. Marinozzi, A. Carotti, **R. Sardella**, F. Buonerba, F. Ianni, B. Natalini, D. Passeri, G. Rizzo, R. Pellicciari. Asymmetric synthesis of the four diastereoisomers of a novel non-steroidal farnesoid X receptor (FXR) agonist: role of the chirality on the biological activity. *Bioorg. Med. Chem.* *21* (2013) 3780.
22. B. Natalini, **R. Sardella**, F. Ianni, M.E. García Rubiño, A. Conejo- García, M. del C. Núñez, M.A. Gallo, J.M. Campos. Chromatographic enantioresolution of six purine derivatives endowed with anti-human breast cancer activity. *Chromatographia* *76* (2013) 475.
23. **R. Sardella**, A. Lisanti, M. Marinozzi, F. Ianni, B. Natalini, G.P. Blanch, M.L. Ruiz del Castillo. Combined monodimensional chromatographic approaches to monitor the presence of D-amino acids in cheese. *Food Control* *34* (2013) 478.
24. A. Macchiarulo, A. Carotti, M. Cellanetti, **R. Sardella**, A. Gioiello. Navigations of chemical space to further the understanding of polypharmacology in human nuclear receptors. *Med. Chem. Comm.* *4* (2013) 216.
25. P. Sabbatini, P. Filippini, **R. Sardella**, B. Natalini, R. Nuti, A. Macchiarulo, R. Pellicciari, A. Gioiello. Synthesis and quantitative structure-property relationships of side chain-modified hyodeoxycholic acid derivatives. *Molecules* *18* (2013) 10497.

27. B. Natalini, **R. Sardella**, F. Ianni. Enantioseparations by High Performance Liquid Chromatography based on Chiral Ligand Exchange, in *Chiral Separations – Methods in Molecular Biology, Methods and Protocols*, 2nd Edition, (Cap. 11), G.K.E. Scriba (Ed.) Humana Press Inc., New York, (J.M. Walker, ser. Ed. ), 2013, 970, 191-208.

### **Comunicazioni degli ultimi 5 anni (2009-2013):**

#### **Orali:**

1. Natalini, **R. Sardella**, A. Macchiarulo, M. Marinozzi, N. Giacchè, R. Pellicciari, Molecular modelling studies in the chiral-ligand exchange chromatography of amino acids. XII International Meeting on Recent Developments in Pharmaceutical Analysis, Milano, Italia, 2009, OC05, 60.
2. B. Natalini, **R. Sardella**, A. Macchiarulo, F. Ianni, R. Pellicciari, Descriptive structure-separation relationship studies in the enantioseparation of amino acids. *Nuove Prospettive in Chimica Farmaceutica – IV Meeting/Workshop*, S. Margherita di Pula, Italia, 2010.
3. B. Natalini, **R. Sardella**, N. Giacchè, F. Ianni, A. Macchiarulo, R. Pellicciari, Computational studies on ligand-exchange systems operating with chiral additives. XXIX Convegno Interregionale Toscana-Umbria-Marche-Abruzzo, Ancona, Italia, 2010, OR10.
4. B. Natalini, **R. Sardella**, F. Ianni, M. E. García Rubiño, A. Carotti, A. Macchiarulo, R. Pellicciari. Mechanistic investigations on a ligand-exchange system operating with a chiral mobile phase. *Nuove Prospettive in Chimica Farmaceutica – V Meeting*, Trieste, 2011, SC28.
5. B. Natalini, **R. Sardella**, A. Gioiello, E. Rosatelli, F. Ianni, E. Camaioni, R. Pellicciari. Fast chromatographic determination of the unconjugated bile salt critical micellar concentration. XIV International Meeting on Recent Developments in Pharmaceutical Analysis, Pavia, 2011, OC20.
6. **R. Sardella**, F. Ianni, A. Lisanti, B. Natalini. Ruolo della fase mobile nell'enantioseparazione con fasi stazionarie chirali a base polisaccaridica. XXXI Congresso Interregionale Toscana-Umbria-Marche-Abruzzo (TUMA) Francavilla al Mare, 2012.
7. **R. Sardella**, F. Ianni, A. Lisanti, B. Natalini. The role of mobile phase in the enantioseparation with polysaccharide-based stationary phases. XXIV International Symposium on

**Altre:**

1. B. Natalini, **R. Sardella**, A. Gioiello, G. Carbone, R. Pellicciari, Side-chain modified bile acids: chromatographic evaluation of the epimer separation. *Nuove Prospettive in Chimica Farmaceutica – III Meeting/Workshop*. Castelvechio Pascoli, Italia, 2009, 114.
2. N. Giacchè, **R. Sardella**, A. Macchiarulo, M. Dawgul, B. Natalini, R. Pellicciari, A new computational model to predict the elution order in the chiral ligand-exchange chromatography (CLEC) of amino acids. *XXIII Congresso Nazionale della Società Chimica Italiana*, Sorrento, Italia, 2009, FAR-PO-79, 177.
3. M.C. Fulco, **R. Sardella**, M. Marinozzi, B. E. Çaliskan, B. Natalini, R. Pellicciari, Synthesis and chromatographic enantioresolution of conformationally constrained analogues of homotaurine. *XXIII Congresso Nazionale della Società Chimica Italiana*, Sorrento, Italia, 2009, FAR-PO-95, 181.
4. E. Camaioni, G. Pittelli, P. Liscio, R. Nuti, A. Macchiarulo, **R. Sardella**, A. Chiarugi, F. Moroni, R. Pellicciari, Combined strategies toward the design and synthesis, of novel inhibitors of indoleamine-2,3-dioxygenase (IDO). *XXIII Congresso Nazionale della Società Chimica Italiana*, Sorrento, Italia, 2009, FAR-PO-13, 160.
5. E. Camaioni, G. Pittelli, P. Liscio, R. Nuti, A. Macchiarulo, **R. Sardella**, A. Chiarugi, F. Moroni, R. Pellicciari, Synthesis, molecular modelling and preliminary evaluation of a series of new thioindantoinine derivatives as inhibitors of indoleamine-2,3-dioxygenase (IDO). *Hungarian-Austrian-Czech-German-Greek-Italian-Polish-Slovak-Slovenian Joint Meeting on Medicinal Chemistry*, Budapest, Ungheria, 2009, P-51, 121.
6. B. Natalini, **R. Sardella**, N. Giacchè, F. Ianni, E. Camaioni, A. Macchiarulo, M. Marinozzi, R. Pellicciari, Chiral ligand-exchange separation and resolution of extremely rigid glutamate analogues: 1-aminospiro[2.2]pentyl-1,4-dicarboxylic acids. *XVI International Symposium on Separation Science*, Roma, Italia, 2010, P11, 86.
7. B. Natalini, **R. Sardella**, A. Gioiello, E. Rosatelli, R. Nuti, E. Camaioni, A. Macchiarulo, R. Pellicciari, Chromatographic hydrophobicity index: a high-throughput tool to estimate the critical micellar concentration of bile acids. *XX National Meeting on Medicinal Chemistry*, Abano Terme, Italia, 2010, P97, 195.
8. B. Natalini, N. Giacchè, **R. Sardella**, F. Ianni, A. Macchiarulo, R. Pellicciari, Computational studies for the elucidation of the enantiomer elution order in chiral ligand-exchange

chromatography. XX National Meeting on Medicinal Chemistry, Abano Terme, Italia, 2010, P98, 196.

9. B. Natalini, F. Ianni, **R. Sardella**, A. Gioiello, P. Sabbatini, P. Filipponi, R. Pellicciari, Chromatographic evaluation of the 25-(*R,S*)-methyl-bishomo-hyodeoxycholic acid epimers. XXIX Convegno Interregionale Toscana-Umbria-Marche-Abruzzo, Ancona, Italia, 2010, OR20.
10. B. Natalini, **R. Sardella**, A. Gioiello, E. Rosatelli, R. Nuti, E. Camaioni, A. Macchiarulo, R. Pellicciari, High-throughput chromatographic determination of the bile acid critical micellar concentration. Drug Analysis 2010, Antwerp, Belgio, 2010, 245, HA02.
11. B. Natalini, **R. Sardella**, S. Massari, F. Ianni, O. Tabarrini, V. Cecchetti. Chromatographic Enantioresolution of Anti-HIV Quinolone Derivatives. XXX Convegno Interregionale Tosco Umbro Marchigiano Abruzzese TUMA 2011, Perugia, Italia, 2011, 32, O15.
12. A. Gioiello, F. Venturoni, **R. Sardella**, B. Natalini, R. Pellicciari (2011). Continuous flow N-acyl amidation of bile acids. In: Frontiers in Medicinal Chemistry Meeting. Stoccolma (Svezia), 19-21 Giugno 2011
13. P. Liscio, E. Camaioni, **R. Sardella**, R. Nuti, A. Macchiarulo, G. Pittelli, A. Chiarugi, F. Moroni, B. Natalini, R. Pellicciari. Synthesis, enantiomeric separation and preliminary evaluation of a series of new thioidantoine derivatives as inhibitors of indoleamine-2,3-dioxygenase (IDO), a novel target for cancer therapy. XXX Convegno Interregionale Tosco Umbro Marchigiano Abruzzese TUMA 2011, Perugia, Italia, 2011, 55, P7.
14. F. Venturoni, A. Gioiello, **R. Sardella**, B. Natalini, R. Pellicciari. Development of an Efficient continuous flow synthesis of glyco- and tauro-conjugated natural and semi-synthetic bile acids. XXIV Congresso Nazionale della Società Chimica Italiana, Lecce, Italia, 2011, 464, FAR-PO-84.
15. B. Natalini, **R. Sardella**, A. Carotti, F. Ianni, M. E. García Rubiño, A. Macchiarulo, R. Pellicciari. The effect of the Cu(II) salt anion in a ligand exchange system operating with a chiral mobile phase. XXIV Congresso Nazionale della Società Chimica Italiana, Lecce, Italia, 2011, 438, FAR-PO-59
16. B. Natalini, F. Ianni, **R. Sardella**, F. Venturoni, A. Gioiello, R. Pellicciari. HPLC/ELSD analysis of conjugated bile acids: a way to assist flow chemistry processes. XXIV Congresso Nazionale della Società Chimica Italiana, Lecce, Italia, 2011, 450, FAR-PO-71.
17. B. Natalini, **R. Sardella**, F. Ianni, M. E. García-Rubiño, A. Conejo-García, M. C. Núñez, J. M. Campos. Chromatographic enantioresolution of six 2- and 6-substituted (*R,S*)-9-(2,3-dihydro-1,4-benzoxathiin-2- or 3-ylmethyl)-9h-purines endowed with anti-human breast cancer activity.

XIV International Meeting on Recent Developments in Pharmaceutical Analysis, Pavia, Italia, 2011, P084.

18. B. Natalini, F. Ianni, **R. Sardella**, A. Lisanti, F. Venturoni, A. Gioiello, R. Pellicciari. Analisi HPLC/ELSD di Acidi Biliari Amidati: un Approccio Efficace Per Assistere Processi Sintetici a Flusso Continuo. XXXI Congresso Interregionale TUMA 2012, Francavilla al Mare (CH), Italia, 2012.
19. B. Natalini, **R. Sardella**, F. Ianni, M.E. García-Rubiño, A. Conejo-García, M.C. Núñez, M.A. Gallo, J.M. Campos. Polysaccharide-Based Enantioresolution of six Purine Derivatives Endowed With Anti-Human Breast Cancer Activity. Nuove Prospettive in Chimica Farmaceutica, NPCF6, Riccione, 2012, 108.
20. B. Natalini, **R. Sardella**, F. Ianni, N. Giacchè, P. Conti, A. Pinto, L. Tamborini. Ligand-exchange enantioresolution of dihydroisoxazole amino acid derivatives. XXI National Meeting on Medicinal Chemistry - NMMC 2012, Palermo, 2012, 122.
21. A. Gioiello, **R. Sardella**, E. Rosatelli, B. Natalini, R. Pellicciari. Novel stereoselective synthesis and chromatographic evaluation of guggulsterones, the bioactive constituents of the hypolipidemic guggulipid. XXI National Meeting on Medicinal Chemistry - NMMC 2012, Palermo, 2012, 131.
22. **R. Sardella**, F. Ianni, A. Lisanti, B. Natalini, G.P. Blanch, M.L. Ruiz del Castillo. Fast Determination of D-Amino Acids in Cheese Extracts With a Coated Chiral Ligand-Exchange Chromatography Stationary Phase. IX Congresso Italiano di Chimica degli Alimenti, ChimALSI 2012, Ischia, 2012, P151 (*Em. J. Food Agric.* **2012**, *24*, 117).
23. A. Gioiello, P. Sabbatini, A. Ogawa, **R. Sardella**, D. Passeri, B. Natalini, G. Robertson, A. Macchiarulo, R. Sommer, R. Pellicciari. Unravelling the molecular basis for DAF-12 activation: diastereoselective synthesis and SAR studies of dafachronic acid derivatives. XXI National Meeting on Medicinal Chemistry, NMMC 2012, Palermo, 2012, 89.
24. A. Gioiello, P. Sabbatini, A. Ogawa, **R. Sardella**, D. Passeri, B. Natalini, G.M. Robertson, A. Macchiarulo, R. Sommer, R. Pellicciari. Unraveling the Molecular Basis for DAF -12 Activation: Diastereoselective Synthesis and SAR Studies of Dafachronic Acid Derivatives. XXII International Symposium on Medicinal Chemistry, EFMC-ISMC 2012, Berlino.
25. F. Ianni, A. Lisanti, **R. Sardella**, M. Marinozzi, B. Natalini. Role of the mobile phase composition in the chromatographic enantioseparation of pharmaceutically relevant compounds. VII AITUN Annual Meeting, "New frontiers in living cell encapsulation", Perugia, 2013, 25.



26. S. Scorzoni, M. Marinozzi, F. Ianni, **R. Sardella**, B. Natalini. Determination of the Pyruvic Acid Content of Three Italian Onion Varieties. VII Meeting Nuove Prospettive in Chimica Farmaceutica, NPCF, Savigliano (CN), 2013, P4.3.
27. **R. Sardella**, A. Lisanti, F. Ianni, B. Natalini. Combined monodimensional chromatographic methods to evaluate the presence of D-amino acids in cheese extracts. XXIV International Symposium on Pharmaceutical and Biomedical Analysis, PBA 2013 - Recent Developments in Pharmaceutical Analysis, RDPA 2013, Bologna, 2013, P1.64.
28. A. Lisanti, **R. Sardella**, F. Ianni, M. Marinozzi, B. Natalini. Approcci cromatografici monodimensionali combinati per determinare la presenza di D-amminoacidi in estratti di formaggi. Convegno interregionale TUMA 2013, Sesto Fiorentino (FI), 2013, OC3.
29. P. Sabbatini, P. Filipponi, **R. Sardella**, B. Natalini, R. Nuti, A. Macchiarulo, R. Pellicciari, A. Gioiello. Side chain modified HDCA derivatives: synthesis, CMC determination and molecular modelling studies. XXII National Meeting on Medicinal Chemistry, Roma, 2013, 111.

#### **Attività didattica A.A. 2013-2014**

Affidamento del Corso di “Analisi Chimico-Farmaceutica I” (3+3L CFU, primo semestre) attivato nell'ambito del Corso di Laurea in Chimica e Tecnologia Farmaceutiche - Università degli Studi di Perugia.