

# Stefano GUGLIELMO, PhD



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## SUMMARY

I am a medicinal chemistry researcher and associate professor at the Department of Drug Science and Technology of the University of Turin, ITALY. I have a documented experience in synthetic medicinal chemistry and a good knowledge in computational chemistry. My research experience is in the field of drug design, with a main interest in cancer therapies and a predominant focus on multi-drug resistance (MDR).

## CORE COMPETENCIES

- Synthetic organic and medicinal chemistry.
- Analytical and spectroscopical methods.
- Molecular mechanics (Amber, NAMD, Gromacs, VMD).
- Basic knowledge of quantum mechanics packages (Orca, GAMESS-US).
- Good knowledge of Unix operating systems and of scripting languages (BASH, TCL, Python).
- **English** Advanced Proficiency.

## EDUCATION AND ACADEMIC EXPERIENCE

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<b>2020-present</b>	<b>Associate professor</b> of Medicinal Chemistry at the Department of Drug Science and Technology (University of Turin).
<b>2012-2020</b>	<b>Assistant professor</b> of Medicinal Chemistry at the Department of Drug Science and Technology (University of Turin). <b>Post-doctoral fellowship</b> at the Department of Drug Science and Technology (University of Turin) Design of novel small molecules endowed with anti-inflammatory, anti-parasitic and anti-cancer activity.
<b>2008-2012</b>	<b>PhD</b> in Drug Science (University of Turin) Design of new anti-parasitic small molecules.
<b>March-june 2007</b>	<b>Doctoral fellowship</b> at the Semmelweis University of Budapest Organic chemistry laboratory (Pr. Matyus)
<b>July 2004</b>	<b>Pharmacist qualification</b>
<b>2004</b>	<b>Master degree</b> in Medicinal Chemistry and Pharmaceutical Technology (University of Turin), <i>summa cum laude</i> and honour mention.

## TEACHING ACTIVITY

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- 2020-present** **Course of Qualitative Drug Analysis 2 (Principles of Organic Synthesis)** (Master Degree in "Medicinal Chemistry and Pharmaceutical Technology" Department of Drug Science and Technology, University of Turin).
- 2014-present** **Course of Qualitative Drug Analysis 1** (Master Degree in "Medicinal Chemistry and Pharmaceutical Technology" Department of Drug Science and Technology, University of Turin).
- AY 2013/2014** **Course of drug extraction and synthesis** (Master Degree in "Medicinal Chemistry and Pharmaceutical Technology" Department of Drug Science and Technology, University of Turin).
- AY 2012/2013** **Course of medicinal chemistry** (Bachelor degree of "Drug Information" Department of Drug Science and Technology, University of Turin).

## PUBLICATIONS

### Journal articles

1. Marini, E.; Rolando, B.; Sodano, F.; Blua, F.; Concina, G.; Guglielmo, S.; Lazzarato, L.; Chegaev, K. Comparative Study of Different H<sub>2</sub>S Donors as Vasodilators and Attenuators of Superoxide-Induced Endothelial Damage. *Antioxidants* 2023, 12, 344. <https://doi.org/10.3390/antiox12020344>
2. L. Braconi, E. Teodori, M. Contino, C. Riganti, G. Bartolucci, D. Manetti, M. N. Romanelli, M. G. Perrone, N. A. Colabufo, S. Guglielmo, S. Dei, Overcoming Multidrug Resistance (MDR): Design, Biological Evaluation and Molecular Modelling Studies of 2,4-Substituted Quinazoline Derivatives. *ChemMedChem* 2022, 17, e202200027. [dx.doi.org/10.1002/cmdc.202200027](https://doi.org/10.1002/cmdc.202200027)
3. Marialessandra Contino, Stefano Guglielmo, Chiara Riganti, Giulia Antonello, Maria Grazia Perrone, Roberta Giampietro, Barbara Rolando, Roberta Fruttero, Nicola A. Colabufo, One molecule two goals: A selective P-glycoprotein modulator increases drug transport across gastro-intestinal barrier and recovers doxorubicin toxicity in multidrug resistant cancer cells, *European Journal of Medicinal Chemistry*, Volume 208, 2020, 112843, [doi.org/10.1016/j.ejmech.2020.112843](https://doi.org/10.1016/j.ejmech.2020.112843)
4. C. Parisi, A. Fraix, S. Guglielmo, F. Spyraakis, B. Rolando, L. Lazzarato, R. Fruttero, A. Gasco, S. Sortino, DNA-Targeted NO Release Photoregulated by Green Light. *Chem. Eur. J.* 2020, 26, 13627. [doi.org/10.1002/chem.202001538](https://doi.org/10.1002/chem.202001538)
5. Sapino, S.; Peira, E.; Chirio, D.; Chindamo, G.; Guglielmo, S.; Oliaro-Bosso, S.; Barbero, R.; Vercelli, C.; Re, G.; Brunella, V.; Riedo, C.; Fea, A.M.; Gallarate, M. Thermosensitive Nanocomposite Hydrogels for Intravitreal Delivery of Cefuroxime. *Nanomaterials* 2019, 9, 1461. <https://doi.org/10.3390/nano9101461>
6. Guglielmo S.; Cortese D.; Cano C.; Fruttero R. Molecular dynamics simulations reveal the determinants of cyclin-dependent kinase 2 inhibition by 5-nitrosopyrimidine derivatives. *Journal of Biomolecular Structure and Dynamics*, 38:13, 4016-4024, DOI: 10.1080/07391102.2019.1666032
7. Chiara Riganti, Marialessandra Contino, \* Stefano Guglielmo,\* Maria G. Perrone, Iris C. Salaroglio, Vladan Milosevic, Roberta Giampietro, Francesco Leonetti, Barbara Rolando, Loretta Lazzarato, Nicola A. Colabufo, Roberta Fruttero. "Design, Biological Evaluation, and Molecular Modeling of Tetrahydroisoquinoline Derivatives: Discovery of A Potent P-Glycoprotein Ligand Overcoming Multidrug Resistance in Cancer Stem Cells." *J. Med. Chem.* **2019**, 62 (2), 974-986.
8. Thais Regina Ferreira de Melo et al. "Discovery of phenylsulfonylfuroxan derivatives as gamma globin inducers by histone acetylation." *Eur. J. Med. Chem.* **2018**, 154, 341-353.
9. Elena Gazzano, Loretta Lazzarato, Barbara Rolando, Joanna Kopecka, Stefano Guglielmo,

Costanzo Costamagna, Konstantin Chegaev,<sup>\*</sup> and Chiara Riganti<sup>1\*</sup> “Mitochondrial Delivery of Phenol Substructure Triggers Mitochondrial Depolarization and Apoptosis of Cancer Cells” *Front. Pharmacol.* **2018**, *9*, 580.

10. Sandra Atlante, Konstantin Chegaev, Chiara Cencioni, Stefano Guglielmo, Elisabetta Marini, Emily Borretto, Carlo Gaetano, Roberta Fruttero, Francesco Spallotta<sup>\*</sup>, Loretta Lazzarato<sup>\*</sup>. “Structural and biological characterization of new hybrid drugs joining an HDAC inhibitor to different NO-donors” *Eur. J. Med. Chem.* **2018**, *144*, 612-625.

11. Viviana Teresa Orlandi<sup>\*</sup>, Fabrizio Bolognese, Barbara Rolando, Stefano Guglielmo, Loretta Lazzarato, Roberta Fruttero. “Anti-*Pseudomonas* activity of 3-nitro-4-phenylfuroxan” *Microbiol.* **2018**, *164*, 1557-1566.

12. Marialessandra Contino,<sup>§</sup> Stefano Guglielmo,<sup>\*§</sup> Maria Grazia Perrone, Roberta Giampietro, Barbara Rolando, Antonio Carrieri, Daniele Zaccaria, Konstantin Chegaev, Vanessa Borio, Chiara Riganti, Katarzyna Zabielska-Koczywas, Nicola A. Colabufo<sup>\*</sup> and Roberta Fruttero. “New tetrahydroisoquinoline-based P-glycoprotein modulators: decoration of the biphenyl core gives selective ligands” *MedChemComm* **2018**, *9*, 862-869.

<sup>§</sup> Equal contribution.

13. Iris Chiara Salaroglio, Elena Gazzano, Joanna Kopecka, Konstantin Chegaev, Costanzo Costamagna, Roberta Fruttero, Stefano Guglielmo,<sup>\*</sup> and Chiara Riganti<sup>\*</sup> “New Tetrahydroisoquinoline Derivatives Overcome Pgp Activity in Brain-Blood Barrier and Glioblastoma Multiforme in Vitro” *Molecules*, **2018**, *23*, 1401.

14. Lorenzo Annaratone, Stefano Guglielmo, Konstantin Yu. Chegaev<sup>\*</sup> “Direct introduction of cyano group on furoxan ring” *Mendel. Comm.* **2017**, *27*, 565-566.

15. Guilherme Felipe dos Santos Fernandes et al. “Design, Synthesis, and Characterization of N-Oxide-Containing Heterocycles with in Vivo Sterilizing Antitubercular Activity” *J. Med. Chem.* **2017**, *60*, 8647-8660.

16. Marco Blangetti, Barbara Rolando, Elisabetta Marini, Konstantin Chegaev, Stefano Guglielmo, Loretta Lazzarato,<sup>\*</sup> Laura Lucarini, Emanuela Masini, and Roberta Fruttero. “*gem*-Dinitroalkyl Benzenes: A Novel Class of IOP-Lowering Agents for the Treatment of Ocular Hypertension” *ACS Med. Chem. Lett.* **2017**, *8*, 1054-1059.

17. Wee Han Poh, Nicolas Barraud, Stefano Guglielmo, Loretta Lazzarato, Barbara Rolando, Roberta Fruttero, and Scott A. Rice<sup>\*</sup>. “Furoxan Nitric Oxide Donors Disperse *Pseudomonas aeruginosa* Biofilms, Accelerate Growth, and Repress Pyoverdine Production” *ACS Chem. Biol.* **2017**, *12*, 2097-2106.

18. Marco Blangetti, Barbara Rolando, Konstantin Chegaev, Stefano Guglielmo, Loretta Lazzarato<sup>\*</sup>, Mariaconcetta Durante, Emanuela Masini, Nicoletta Almirante, Elena Bastia, Francesco Impagnatiello,

Roberta Fruttero, Alberto Gasco. "New furoxan derivatives for the treatment of ocular hypertension" *Bioorg. Med. Chem. Lett.* **2017**, 27, 479-483.

19. Stefano Guglielmo\*, Loretta Lazzarato, Marialessandra Contino, Maria G. Perrone, Konstantin Chegaev, Antonio Carrieri, Roberta Fruttero, Nicola A. Colabufo, Alberto Gasco. "Structure-Activity Relationship Studies on Tetrahydroisoquinoline Derivatives: [4'-(6,7-Dimethoxy-3,4-dihydro-1H-isoquinolin-2-ylmethyl)biphenyl-4-ol] (MC70) Conjugated through Flexible Alkyl Chains with Furazan Moieties Gives Rise to Potent and Selective Ligands of P-glycoprotein." *J. Med. Chem.* **2016** 59 6729-6738.

20. Stefano Guglielmo\*, Marialessandra Contino, Loretta Lazzarato, Maria Grazia Perrone, Marco Blangetti, Roberta Fruttero, Nicola A. Colabufo. "A Potent and Selective P-gp Modulator for Altering Multidrug Resistance Due to Pump Overexpression." *ChemMedChem* **2016** 11 374-376.

21. Roberta Fruttero, Marco Crosetti, Konstantin Chegaev, Stefano Guglielmo, Alberto Gasco, Francesco Berardi, Mauro Niso, Roberto Perrone, Maria Antonietta Panaro, Nicola Antonio Colabufo. "Phenylsulfonylfuroxans as Modulators of Multidrug-Resistance-Associated Protein-1 and P-Glycoprotein" *J. Med. Chem.* **2010** 15 611-621.

22. Aurore Fraix<sup>§</sup>, Stefano Guglielmo<sup>§</sup>, Venera Cardile, Adriana C. E. Graziano, Ruxandra Gref, Barbara Rolando, Roberta Fruttero, Alberto Gasco, Salvatore Sortino. "A multi-photoresponsive molecular-hybrid for dual-modal photoinactivation of cancer cells." *RSC Adv* **2014** 4 44827-44836.

<sup>§</sup> Equal contribution.

23. Stefano Guglielmo, Daniela Cortese, Francesca Vottero, Barbara Rolando, Valerie P. Kommer, David L. Williams, Roberta Fruttero, Alberto Gasco. "New Praziquantel Derivatives Containing NO-donor Furoxans and Related Furazans as Active Agents against *Schistosoma mansoni*." *Eur. J. Med. Chem.* **2014** 84 135-145.

24. Stefano Guglielmo, Massimo Bertinaria, Barbara Rolando, Marco Crosetti, Roberta Fruttero, Vanessa Yardley, Simon L. Croft, Alberto Gasco. "A new series of amodiaquine analogues modified in the basic side chain with in vitro antileishmanial and antiplasmodial activity" *Eur. J. Med. Chem.* **2009** 44 5071-5079.

25. Massimo Bertinaria<sup>§</sup>, Stefano Guglielmo<sup>§</sup>, Barbara Rolando, Marta Giorgis, Cristina Aragno, Roberta Fruttero, Alberto Gasco, Silvia Parapini, Donatella Taramelli, Yuri C. Martins, Leonardo J.M. Carvalho. "Amodiaquine analogues containing NO-donor substructures: Synthesis and their preliminary evaluation as potential tools in the treatment of cerebral malaria" *Eur. J. Med. Chem.* **2011** 46 1757-

1767.

<sup>§</sup> Equal contribution.

26. Massimo Bertinaria, Pamela Orjuela-Sanchez, Elisabetta Marini, Stefano Guglielmo, Anthony Hofer, Yuri C. Martins, Graziela M. Zanini, John A. Frangos, Alberto Gasco, Roberta Fruttero, Leonardo J. M. Carvalho. "NO-Donor Dihydroartemisinin Derivatives as Multitarget Agents for the Treatment of Cerebral Malaria." *J. Med. Chem.* **2015** 58 7895-7899.

27. Konstantin Chegaev, Chiara Riganti, Loretta Lazzarato, Barbara Rolando, Stefano Guglielmo, Ivana Campia, Roberta Fruttero, Amalia Bosia, Alberto Gasco. "Nitric Oxide Donor Doxorubicins Accumulate into Doxorubicin-Resistant Human Colon Cancer Cells Inducing Cytotoxicity" *ACS Med. Chem. Lett.* **2011** 2 494-497.

28. Konstantin Chegaev, Chiara Riganti, Barbara Rolando, Loretta Lazzarato, Elena Gazzano, Stefano Guglielmo, Dario Ghigo, Roberta Fruttero, Alberto Gasco. "Doxorubicin-antioxidant multitarget drugs" *Bioorg. Med. Chem. Lett.* **2013** 23 5307-5310.

29. Massimo Bertinaria, Barbara Rolando, Marta Giorgis, Gabriele Montanaro, Stefano Guglielmo, M. Federica Buonsanti, Valentina Carabelli, Daniela Gavello, Pier Giuseppe Daniele, Roberta Fruttero, Alberto Gasco. "Synthesis, Physicochemical Characterization, and Biological Activities of New Carnosine Derivatives Stable in Human Serum As Potential Neuroprotective Agents" *J. Med. Chem.* **2011** 54 611-621.

30. Loretta Lazzarato, Konstantin Chegaev, Elisabetta Marini, Barbara Rolando, Emily Borretto, Stefano Guglielmo, Sony Joseph, Antonella Di Stilo, Roberta Fruttero, and Alberto Gasco. "New Nitric Oxide or Hydrogen Sulfide Releasing Aspirins" *J. Med. Chem.* **2011** 54 5478-5484.

31. Luiz Antônio Dutra, Letícia de Almeida, Thais G. Passalacqua, Juliana Santana Reis, Fabio A. E. Torres, Isabel Martinez, Rosangela Gonçalves Peccinini, Chung Man Chin, Konstantin Chegaev, Stefano Guglielmo, Roberta Fruttero, Marcia A. S. Graminha, Jean Leandro dos Santos. "Leishmanicidal Activities of Novel Synthetic Furoxan and Benzofuroxan Derivatives." *Antimicrob. Agents Chemother.* **2014** 58 4837-4847.

32. Guilherme F. dos Santos Fernandes, Paula C. de Souza, Leonardo B. Marino, Konstantin Chegaev, Stefano Guglielmo, Loretta Lazzarato, Roberta Fruttero, Man C. Chung, Fernando R. Pavan, Jean Leandro dos Santos. "Synthesis and biological activity of furoxan derivatives against *Mycobacterium tuberculosis*." *Eur. J. Med. Chem.* **2016** 123 523-531.

33. Aurore Fraix, Marco Blangetti, Stefano Guglielmo, Loretta Lazzarato, Nino Marino, Venera Cardile,

Adriana C. E. Graziano, Ilse Manet, Roberta Fruttero, Alberto Gasco, Salvatore Sortino. "Light-Tunable Generation of Singlet Oxygen and Nitric Oxide with a Bichromophoric Molecular Hybrid: a Bimodal Approach to Killing Cancer Cells." *ChemMedChem* **2016** *11* 1371-1379.

34. Daniela Cortese, Konstantin Chegaev, Stefano Guglielmo, Lan Z. Wang, Bernard T. Golding, Céline Cano, Roberta Fruttero. "Synthesis and Biological Evaluation of N<sub>2</sub>-Substituted 2,4-Diamino-6-cyclohexylmethoxy-5-nitrosopyrimidines and Related 5-Cyano-NNO-azoxy Derivatives as Cyclin-Dependent Kinase 2 (CDK2) Inhibitors." *ChemMedChem* **2016** *11* 1705-1709.

35. Lucía Boiani, Gabriela Aguirre, Mercedes Gonzalez, Hugo Cerecetto, Agustina Chidichimo, Juan J. Cazzulo, Massimo Bertinaria, Stefano Guglielmo. "Furoxan-, alkylnitrate-derivatives and related compounds as anti-trypanosomatid agents: Mechanism of action studies" *Bioorg. Med. Chem.* **2008** *16* 7900-7907.

36. Marco Blangetti, Barbara Rolando, Konstantin Chegaev, Stefano Guglielmo, Loretta Lazzarato, Mariaconcetta Durante, Emanuela Masini, Nicoletta Almirante, Elena Bastia, Francesco Impagnatiello, Roberta Fruttero, Alberto Gasco. "New furoxan derivatives for the treatment of ocular hypertension." *Bioorg. Med. Chem. Lett.* **2017** *27* 479-483.

37. Donatella Boschi, Stefano Guglielmo, Stefania Aiello, Giulia Morace, Elisa Borghi, Roberta Fruttero. "Synthesis and in vitro antimicrobial activities of new (cyano-NNO-azoxy) pyrazole derivatives" *Bioorg. Med. Chem. Lett.* **2011** *21* 3431-3434.

38. Loretta Lazzarato, Clara Cena, Barbara Rolando, Elisabetta Marini, Marco Lucio Lolli, Stefano Guglielmo, Elena Guaita, Giuseppina Morini, Gabriella Coruzzi, Roberta Fruttero, Alberto Gasco. "Searching for new NO-donor aspirin-like molecules: Furoxanylacyl derivatives of salicylic acid and related furazans" *Bioorg. Med. Chem.* **2011** *19* 5852-5860.

39. Yasinalli Tamboli; Loretta Lazzarato; Elisabetta Marini; Stefano Guglielmo; Michela Novelli; Pascale Befly; Pellegrino Masiello; Roberta Fruttero; Alberto Gasco. "Synthesis and preliminary biological profile of new NO-donor tolbutamide analogues." *Bioorg. Med. Chem. Lett.* **2012** *22* 3810-3815.

40. Antonia Patruno, Paolo Tosco, Emily Borretto, Sara Franceschelli, Paolo Amerio, Mirko Pesce, Stefano Guglielmo, Pietro Campiglia, Maria Grazia Bernengo, Roberta Fruttero. "Thymopentin down-regulates both activity and expression of iNOS in blood cells of Sézary syndrome patients" *Nitric Oxide* **2012** *27* 143-149.

41. Maria Elisa Crestoni, Barbara Chiavarino, Stefano Guglielmo, Valentina Lilla, Simonetta Fornarini "Tandem Mass Spectrometry of Nitric Oxide and Hydrogen Sulfide Releasing Aspirins: A Hint into Activity

Behavior" *Mass Spectrom* **2013** 2 A0017-1- A0017-4.

42. Konstantin Chegaev, Barbara Rolando, Stefano Guglielmo, Roberta Fruttero, Alberto Gasco. "Unsymmetrically Substituted Furoxans. Part 19. Methyl and Phenylfuroxansulfonic Acids and Related Sulfonamides" *J. Heterocyclic Chem.* **2009** 866-872.

#### Oral communications

1. From activity to mechanism: understanding interaction of small molecules with P-glycoprotein through enhanced sampling molecular dynamics. 2019 6th CDDD Meeting - COMPUTATIONALLY DRIVEN DRUG DISCOVERY.
2. EFFICIENTLY TARGETING DRUG EFFLUX THROUGH MODULATION OF P-GLYCOPROTEIN ACTIVITY BY SMALL MOLECULES: DESIGN, BIOLOGICAL AND COMPUTATIONAL STUDY. 21st Transporter and Barrier Meeting. Bad Herrenalb, 2019 may 27th-29<sup>th</sup>.
3. Potent and Selective P-gp Modulators for Altering Multidrug Resistance Due to Pump Overexpression. XXIV National Meeting on Medicinal Chemistry & Nuove Prospettive in Chimica Farmaceutica 10, Perugia, September 11-16 2016.
4. Synthesis of Amodiaquine Analogues with Potential Antiprotozoal Activity. XXVII Advanced Course of Medicinal Chemistry and "E. Duranti" National Seminar for PhD Students, Urbino, July 1-6 2007.

#### Poster presentations

1. Guglielmo, S. et al. "Phenylsulfonyl Furoxans as Modulators of Multidrug Resistance-associated Protein-1 and P-glycoprotein." XX National Meeting on Medicinal Chemistry, Abano Terme, Padova September 12-16 2010. P113.
2. Guglielmo, S. et al. "Praziquantel analogues containing NO-donor furoxans and related furazans as agents active against *Schistosoma mansoni*." XXIV Congresso Nazionale della Società Chimica Italiana. Lecce, September 11-16 2011. Atti del congresso. p. 418.
3. Guglielmo S. et al. "New potent and selective P-gp inhibitors." Nuove Prospettive in Chimica Farmaceutica 7, Savigliano (CN), May 29-31 2013. Poster P1.13.