ROBERTA FRUTTERO

Curriculum Vitae

Personal data

- Born in Torino - 14/12/1952
- Nationality: Italian
- Affiliation: Department of Drug Science and Technology, University of Torino, via Pietro Giuria 9, 10125 Torino, Italy tel.: +390116707850; fax: +390116707826;
- email: roberta.fruttero@unito.it

Curriculum studiorum:

-1977 Degree in Pharmaceutical Chemistry and Technology at the University of Torino
-1978 Degree in Pharmacy

Professional Curriculum

1980 Assistant Professor of Medicinal Chemistry at the Faculty of Pharmacy of the University of Torino
1992 Associated Professor of Medicinal Chemistry at the Faculty of Pharmacy of the University of Sassari,
1994 Full Professor of Medicinal Chemistry at the Faculty of Pharmacy of the University of Torino.
1997-2003 Member of the National Medicinal Chemistry Committee.
1998-2009 Director of the PhD course in Pharmaceutical Sciences at the Doctorate School of Science and High Technology of the University of Torino.
2001-2007 Director of the undergraduate course in Herbal Medicine Technology.
2002-2011 Member of the Committee of the European School of Medicinal Chemistry (ESMEC).
Since 2012 at present Director of the School of Hospital Pharmacy.

Stages and Visiting Professor

Queen Mary College in London (Prof. E. Randall); Zurich University (Professor W. Von Philipsborn); Borstel Research Institute (Prof. J.Seydel); N. D. Zelinsky Institute of Organic Chemistry Russian Academy of Sciences; School of Pharmacy at University of Lausanne (Prof. Bernard Testa); Department of Pharmaceutical Sciences University of Geneve (Prof. Pierre-Alain Carrupt).

Recent Teaching experiences

Professor of *Medicinal Chemistry* at the Department of Drug Science and Technology (UNITO)
Professor of *Methods for Herbal Medicine Analysis* at Herbal Medicine Technology Course (UNITO)
Professor of *Molecular Basis for Drug-Drug Interaction* at the School of Hospital Pharmacy (UNITO)

Scientific activity

The scientific activity, collected in more than 190 publications, is in the field of drug design and mainly concerns the development of novel furoxan, nitric ester, nitrosothiol, diazeniumdiolate as NO-donors and their biological and pharmacological characterization. The use of NO-donors in the design of polyvalent agents (multitarget agents) of interest in many therapeutic areas is one of the main aim of her research. More recently MDR anticancer agents have been focused.
The h index for the papers is 32 as calculated by Scopus on the 5/3/2019.

Collaborations

Nicox Research (Sophie Antipolis, France)
Laboratoire de Chimie Thérapeutique - Pharmacochimie (Université de Genève, Switzerland)
Institute des Sciences Moléculaires de Marseille (Université Aix-Marseille, France)
La Jolla Bioengineering Institute, (San Diego, California, USA)
Department of Immunology/Microbiology (Rush University Medical Center, Chicago, Illinois, USA)
Department of Oncology - School of Medicine (University of Turin, Italy)
MRC Centre for Inflammation Research (University of Edinburgh, UK)
Department of Diabetes and Cardiovascular Science - Centre for Health Science (University of the Highlands and Islands - UK)
Department of Drug Science (University of Bari –Italy)

Faculdade de Ciências Farmacêuticas – Universidade Estadual Paulista–UNESP, Rodovia Araraquara Jaú Km. 01, 14801-902, Araraquara, SP, Brazil.
Department of Drug Science and Technology (*University of Catania – Italy)*

Recent publications

1. Parisi, C; Failla, MC; Fraix, A.; Rescifina, A.; Rolando, B.; Lazzarato, L.; Cardile, V.; Graziano, A.C. E.; Fruttero, R.; Gasco, A.; Sortino, S. A molecular hybrid producing simultaneously singlet oxygen and nitric oxide by single photon excitation with green light. *Bioorganic chemistry*, 2019, 85, 18-22
2. Buondonno I, Gazzano E., Tavanti E., Chegaev K., Kopecka J., Fanelli M., Rolando B., Fruttero R., Gasco A., Hattinger C., Serra M., Riganti C. Endoplasmic reticulum-targeting doxorubicin: a new tool effective against doxorubicin-resistant osteosarcoma. *Cell Mol Life Sci.* 2019, 76, 609-625
3. Riganti C, Contino M, Guglielmo S, Perrone MG, Salaroglio IC, Milosevic V, Giampietro R, Leonetti F, Rolando B, Lazzarato L, Colabufo NA, Fruttero R. Design, Biological Evaluation and Molecular Modelling of Tetrahydroisoquinoline Derivatives: Discovery of A Potent P-glycoprotein Ligand Overcoming Multi-Drug Resistance in Cancer Stem Cells. *J. Med. Chem.*, 2019, 62, 974, 986
4. Sodano, F.: Gazzano, E.; Fraix, A.; Rolando, B.; Lazzarato, L.; Russo, M.; Blangetti, M.; Riganti, C.; Fruttero, R.; Gasco, A.; Sortino, S.. A Molecular Hybrid for Mitochondria-Targeted NO Photodelivery, *CHEMMEDCHEM*, 2018, 13, 87-96
5. Orlandi, V.T.; Bolognese, F.; Rolando, B.; Guglielmo, S.; Lazzarato, L.; Fruttero, R. Anti-pseudomonas activity of 3-nitro-4-phenylfuroxan, *Microbiology*, 2018, 164, 1557-1566
6. Risso V, Farran D, Javierre G, Naubron JV, Giorgi M, Piras P, Jean M, Vanthuyne N, Fruttero R, Lorcy D, Roussel C. Atropoisomerism in a ten-membered ring with multiple chirality axes: (3Z,9Z)-1,2,5,8-dithiadiazecine-6,7(5H,8H)-dione series. *J Org Chem*. 2018 Jun 8. doi: 0.1021/acs.joc. 8b01009.
7. Sodano F, Rolando B, Spyrakis F, Failla M, Lazzarato L, Gazzano E, Riganti C, Fruttero R, Gasco A, Sortino S. Tuning the Hydrophobicity of a Mitochondria-Targeted NO Photodonor. *ChemMedChem*. 2018 Apr 6. doi: 10.1002/cmdc.201800088.
8. Melo TRF, Kumkhaek C, Fernandes GFDS, Lopes Pires ME, Chelucci RC, Barbieri KP, Coelho F, Capote TSO, Lanaro C, Carlos IZ, Marcondes S, Chegaev K, Guglielmo S, Fruttero R, Chung MC, Costa FF, Rodgers GP, Dos Santos JL. Discovery of phenylsulfonylfuroxan derivatives as gamma globin inducers by histone acetylation. *Eur J Med Chem.* 2018, 154, 341-353.
9. Atlante S, Chegaev K, Cencioni C, Guglielmo S, Marini E, Borretto E, Gaetano C, Fruttero R, Spallotta F, Lazzarato L. Structural and biological characterization of new hybrid drugs joining an HDAC inhibitor to different NO-donors. *Eur J Med Chem.* 2018 Jan 20;144:612-625
10. Gazzano E, Rolando B, Chegaev K, Salaroglio IC, Kopecka J, Pedrini I, Saponara S, Sorge M, Buondonno I, Stella B, Marengo A, Valoti M, Brancaccio M, Fruttero R, Gasco A, Arpicco S, Riganti C. Folate-targeted liposomal nitrooxy-doxorubicin: An effective tool against P-glycoprotein-positive and folate receptor-positive tumors. J Control Release, 2018; 270, 37-52
11. Sodano F, Gazzano E, Fraix A, Rolando B, Lazzarato L, Russo M, Blangetti M, Riganti C, Fruttero R, Gasco A, Sortino S. A Molecular Hybrid for Mitochondria-Targeted NO Photodelivery. *ChemMedChem.* 2018; 13, 87-96.
12. Blangetti M, Rolando B, Marini E, Chegaev K, Guglielmo S, Lazzarato L, Lucarini L, Masini E, **Fruttero R.** *gem*-Dinitroalkyl Benzenes: A Novel Class of IOP-Lowering Agents for the Treatment of Ocular Hypertension. *ACS Med Chem Lett*. 2017; 8, 1054-1059.
13. Dos Santos Fernandes GF, de Souza PC, Moreno-Viguri E, Santivañez-Veliz M, Paucar R, Pérez-Silanes S, Chegaev K, Guglielmo S, Lazzarato L, Fruttero R, Man Chin C, da Silva PB, Chorilli M, Solcia MC, Ribeiro CM, Silva CSP, Marino LB, Bosquesi PL, Hunt DM, de Carvalho LPS, de Souza Costa CA, Cho SH, Wang Y, Franzblau SG, Pavan FR, Dos Santos JL. Design, Synthesis, and Characterization of N-Oxide-Containing Heterocycles with in Vivo Sterilizing Antitubercular Activity. *J Med Chem.* 2017; 60, 8647-8660.

14. Blangetti M, Fraix A, Lazzarato L, Marini E, Rolando B, Sodano F, Fruttero R, Gasco A, Sortino S. A Nonmetal-Containing Nitric Oxide Donor Activated with Single-Photon Green Light. *Chemistry*. *2017* ; 23 9026-9029
15. Poh WH, Barraud N, Guglielmo S, Lazzarato L, Rolando B, Fruttero R, Rice SA. Furoxan Nitric Oxide Donors Disperse Pseudomonas aeruginosa Biofilms, Accelerate Growth, and Repress Pyoverdine Production. *ACS Chem Biol. 2017*; 12, 2097-2106
16. Chegaev K, Fraix A, Gazzano E, Abd-Ellatef GE, Blangetti M, Rolando B, Conoci S, Riganti C, Fruttero R, Gasco A, Sortino S.Light-Regulated NO Release as a Novel Strategy To Overcome Doxorubicin Multidrug Resistance. *ACS Med Chem Lett. 2017*; 8, 361-365
17. Blangetti M, Rolando B, Chegaev K, Guglielmo S, Lazzarato L, Durante M, Masini E, Almirante N, Bastia E, Impagnatiello F, Fruttero R, Gasco A. New furoxan derivatives for the treatment of ocular hypertension. *Bioorg Med Chem Lett. 2017*; 27, 479-483
18. Gazzano E, Chegaev K, Rolando B, Blangetti M, Annaratone L, Ghigo D, Fruttero R, Riganti C. Overcoming multidrug resistance by targeting mitochondria with NO-donating doxorubicins. *Bioorg Med Chem. 2016*; 24, 967-75.
19. Chegaev K, Rolando B, Cortese D, Gazzano E, Buondonno I, Lazzarato L, Fanelli M, Hattinger CM, Serra M, Riganti C, Fruttero R, Ghigo D, Gasco A. H2S-Donating Doxorubicins May Overcome Cardiotoxicity and Multidrug Resistance. *J Med Chem. 2016*; 26, 4881-9
20. Fernandes GF, de Souza PC, Marino LB, Chegaev K, Guglielmo S, Lazzarato L, Fruttero R, Chung MC, Pavan FR, Dos Santos JL. Synthesis and biological activity of furoxan derivatives against Mycobacterium tuberculosis. *Eur J Med Chem. 2016*, 123, 523-31.
21. Fraix, A.; Blangetti, M.; Guglielmo, S.; Lazzarato, L.; Marino, N.; Cardile, V.; Graziano, A. C. E.; Manet, I.; Fruttero, R.; Gasco, A.; Sortino, S., Light-Tunable Generation of Singlet Oxygen and Nitric Oxide with a Bichromophoric Molecular Hybrid: a Bimodal Approach to Killing Cancer Cells. *ChemMedChem 2016*, DOI: 10.1002/cmdc.201500396.
22. Guglielmo S, Contino M, Lazzarato L, Perrone MG, Blangetti M, Fruttero R, Colabufo NA., A Potent and Selective P-gp Modulator for Altering Multidrug Resistance Due to Pump Overexpression. *ChemMedChem. 2016*; 11, 374-6
23. Cortese D, Chegaev K, Guglielmo S, Wang LZ, Golding BT, Cano C, Fruttero R. Synthesis and Biological Evaluation of N(2) -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, 1705-8.
24. Guglielmo S, Lazzarato L, Contino M, Perrone MG, Chegaev K, Carrieri A, Fruttero R, Colabufo NA, Gasco A. 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, 6729-38
25. Hoxha, M.; Buccellati, C.; Capra, V.; Carnevali, S.; Sala, A.; Garella, D.; Cena, C.; Rolando, B.; Fruttero, R.; Bertinaria, M.; Rovati, G. E., In vitro pharmacological evaluation of multitarget agents for thromboxane prostanoid receptor antagonism and COX-2 inhibition. *Pharmacol Res. 2016, 103, 132–143*
26. Bertinaria, M.; Orjuela-Sanchez, P.; Marini, E.; Guglielmo, S.; Hofer, A.; Martins, Y. C.; Zanini, G. M.; Frangos, J. A.; Gasco, A.; Fruttero, R.; Carvalho, L. J. M., NO-Donor Dihydroartemisinin Derivatives as Multitarget Agents for the Treatment of Cerebral Malaria. *J. Med. Chem. 2015*, 58, 7895-7899.
27. Chegaev, K.; Federico, A.; Marini, E.; Rolando, B.; Fruttero, R.; Morbin, M.; Rossi, G.; Fugnanesi, V.; Bastone, A.; Salmona, M.; Badiola, N. B.; Gasparini, L.; Cocco, S.; Ripoli, C.; Grassi, C.; Gasco, A., NO-donor thiacarbocyanines as multifunctional agents for Alzheimer's disease. *Bioorg. Med. Chem. 2015*, 23, 4688-4698.
28. Chiazza, F.; Chegaev, K.; Rogazzo, M.; Benetti, E.; Lazzarato, L.; Fruttero, R.; Collino, M.; Cutrin, J. C., A nitric oxide-donor furoxan moiety improves the efficacy of edaravone against early renal dysfunction and injury evoked by ischemia/reperfusion. *Oxid Med Cell Longev 2015*, (Copyright (C) 2015 U.S. National Library of Medicine.), 804659.
29. Chegaev, K.; Lazzarato, L.; Tamboli, Y.; Boschi, D.; Blangetti, M.; Scozzafava, A.; Carta, F.; Masini, E.; Fruttero, R.; Supuran, C. T.; Gasco, A., Furazan and furoxan sulfonamides are strong

α-carbonic anhydrase inhibitors and potential antiglaucoma agents. *Bioorg. Med. Chem. 2014*, 22, 3913-3921.
30. Dutra, L. A.; de Almeida, L.; Passalacqua, T. G.; Reis, J. S.; Torres, F. A. E.; Martinez, I.; Peccinini, R. G.; Chin, C. M.; Chegaev, K.; Guglielmo, S.; Fruttero, R.; Graminha, M. A. S.; dos Santos, J. L., Leishmanicidal activities of novel synthetic furoxan and benzofuroxan derivatives. Antimicrob. *Agents Chemother. 2014*, 58, 4837-4847
31. Fraix, A.; Guglielmo, S.; Cardile, V.; Graziano, A. C. E.; Gref, R.; Rolando, B.; Fruttero, R.; Gasco, A.; Sortino, S., A multi-photoresponsive molecular-hybrid for dual-modal photoinactivation of cancer cells. *RSC Adv. 2014*, 4, 44827-44836.
32. Guglielmo, S.; Cortese, D.; Vottero, F.; Rolando, B.; Kommer, V. P.; Williams, D. L.; Fruttero, R.; Gasco, A., New praziquantel derivatives containing NO-donor furoxans and related furazans as active agents against Schistosoma mansoni. *Eur. J. Med. Chem. 2014*, 84, 135-145.
33. Tasso, B.; Pirisino, G.; Novelli, F.; Garzon, D.; Fruttero, R.; Sparatore, F.; Colombo, V.; Sironi, A., On the self-condensation of aminoguanidine leading to 1,1,4,10,10-pentaamino-2,3,5,6,8,9-hexaazadeca-1,3,5,7,9-pentaene . *Tetrahedron 2014*, 70, 8056-8061.
34. Pedrini, I.; Gazzano, E.; Chegaev, K.; Rolando, B.; Marengo, A.; Kopecka, J.; Fruttero, R.; Ghigo, D.; Arpicco, S.; Riganti, C., Liposomal Nitrooxy-Doxorubicin: One Step over Caelyx in Drug-Resistant Human Cancer Cells. *Mol. Pharmaceutics 2014*, 11, 3068-3079.

Patents

Blangetti, M.; Fruttero, R.; Gasco, A.; Giorgis, M.; Lazzarato, L.; Rolando, B.; Almirante, N.; Storoni, L. "Quinone based nitric oxide donating compounds", WO2015155234 A1, PCT/EP2015/057611, Oct 15, 2015.
Blangetti, M.; Fruttero, R.; Gasco A.; Colabufo N. et al. "Nuovi Derivati Ossadiazolici come Inibitori Selettivi della Glicoproteina-P (gp-P)". BI4739R n. di deposito RM2014A000295
Bertinaria, M.; De Moura Carvalho, L. J.; Fruttero, R.; Gasco, A. Preparation of a hybrid compound for the treatment of cerebral malaria. IT1416933B1, 2015.
Enzo Bronte, Marco Crosetti, Loretta Lazzarato, Roberta Fruttero, Alberto Gasco, Antonella Viola (2013) Novel water soluble furoxan derivatives having antitumor activity**,** n°brevetto: US20130035360 A1.
Konstantin Chegaev, Daniela Cortese, Roberta Fruttero, Alberto Gasco, Elena Gazzano, Barbara Rolando, Chiara Riganti, Vladimir Vladimirovich Novakovskiy (In corso di stampa/deposito) Derivatives of doxorubicin to treat malignant neoplasms, application number 61/911,171, filing date of December 3, 2013.
Alberto Gasco, Roberta Fruttero, Loretta Lazzarato, Barbara Rolando, Konstantin Chegaev, Monica Donnola, Ennio Ongini, Stefano Biondi (2009) NO-donor aspirin derivatives, n°brevetto: WO2010118968.
Antonella Viola, Enzo Bronte, Marco Crosetti, Loretta Lazzarato, Roberta Fruttero, Alberto Gasco (2009) Nitric Oxide furoxan derivative compounds endowed with antitumoral activity, n° brevetto: WO2010081877.
Roberta Fruttero; Alberto Gasco; Loretta Lazzarato; Monica Donnola; Barbara Rolando, Stefano Biondi (2009) New NO-donor aspirin derivatives, n° brevetto: WO2009/049961.
Roberta Fruttero; Alberto Gasco; Loretta Lazzarato; Monica Donnola; Barbara Rolando, (2007) Salicilic acid derivatives, n°brevetto: WO07060112.