Curriculum Vitae
Simona Rapposelli

PERSONAL DATA AND ADDRESS
Nationality: Italian
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ACADEMIC CAREER

July 2017	Licence as Full Professor in Medicinal chemistry
Dec 2015-	**Associate Professor** in Medicinal Chemistry
November 2014	**Visiting Researcher** at the School of Pharmaceutical Sciences of Sun Yat-Sen University (Guangzhou, China)
January 2014	Licence as Associate Professor in Medicinal Chemistry
Dec 2007–2015	**Assistant Professor** at the Department of Pharmaceutical Sciences of the Faculty of Pharmacy of the University of Pisa.
May 2003–Dec 2007	**Research Associate** in the Medicinal Chemistry Laboratory at the University of Pisa with Professor Aldo Balsamo.
Jan 2000–May 2003	**Ph.D. in Medicinal Chemistry** (Dottorato di Ricerca in "Scienza del farmaco e delle sostanze bioattive") with the thesis "Design and Synthesis of new non-steroidal antiinflammatory molecules as selective ciclooxygenase 2 inhibitors", Department of Pharmaceutical Sciences, University of Pisa (Italy). Supervisor: Prof. Aldo Balsamo
Nov 2001	State Examination for Professional Qualification as Pharmacist
Nov 12, 1999	Thesis Defence Supervisor: Professor Aldo Balsamo
1993–1999	Degree in Pharmaceutical Chemistry and Technology (CTF) Thesis title: Oxime-derivatives as inhibitors of ciclooxygenase 2 enzyme: effects on the activity of chemical manipulations Department of Pharmaceutical Sciences, University of Pisa (Italy).

TEACHING ACTIVITY

<u>in Degree programs (University of Pisa):</u>
Medicinal Chemistry II
Narcotic and Antiinflammatory Drugs
Antiinflammatory Drugs and Vitamins
Laboratory course of "Analysis of Drugs"
Analitical Chemistry
Synthesis in medicinal Chemistry
Innovative synthetic strategies in medicinal chemistry

<u>in Master Degree (University of Pisa):</u>
Chemistry and SAR of Drugs (SFIF)
Bioavailability of Drugs (SFIF)
Design of new multitarget drugs: medicinal chemistry strategies (for the II level Master "Regulatory Activities: Drugs, health products, Advanced Therapies and REACH")
In PhD School (University of Pisa and Joint-PhD Programs):

New pharmacological targets for the hypertension therapy: medicinal chemistry approaches (Joint PhD program Universities of Pisa, Siena, Camerino, Firenze and Perugia)
Synthetic strategies to develop new multitarget drugs (PhD in Science of Drugs and Bioactive Substances)
Targeted Therapy (PhD in Science of Drugs and Bioactive Substances)
Anticancer Drugs (school of "Farmacia ospedaliera")

ORAL COMMUNICATIONS

(2008) - *Spiro-heterocyclic benzopyran derivatives: New activators of mitoKATP channels as potential cardioprotective agents.* XIII Meeting on Heterocyclic structures in Medicinal Chemistry, vol. abstracts, **invited lecture**, pp189-200, Palermo, may 18-21

(2009) - *Spirocyclic Benzopyran-based derivatives as new anti-ischemic activators of mitochondrial ATP-sensitive potassium channel (mito-K_{ATP}).* XXIII Congresso Nazionale della Società Chimica Italiana, **Premio Farmindustria 2009**, Sorrento, July 5-10

(2014) - *Multitarget strategies in drug discovery: the dawn of H_2S-donor chimeras for therapeutic purposes.* Invited lecture November 5th, 2014 Sun Yan-Set University Guangzhou (China)

Academic Review

2010	Book "Multifunctional drugs : new chimeras in medicinal chemistry and drug discovery" - **Guest Editor** Research SignPost
2010	Current Topics in Medicinal Chemistry - **Guest Editor**
2006 – present	**Journal reviews**: J. Med. Chem.; J. Pharmacy and Pharmacology; Bioorg. Med. Chem.; Bioorg. Med. Chem. Lett.; Expert Opinion On Drug Metabolism & Toxicology; The Open Biomarkers Journal; European journal of medicinal chemistry; Archiv der Pharmazie; Antioxidants and Redox Signaling; ACS Medicinal Chemistry Letters)
2011 – 2016	**Editorial Board Member** of TheScientificWorldJournal
2012	**External Reviewer** of research proposals submitted to the Portuguese Foundation for Science and Technology (FCT):Life&Health Sciences 2012
2012 – 2017	**Reviewer** of research proposals submitted to national calls (PRIN2012,Futuro in Ricerca 2013, PRIN2015)
2013	**Member of Technical Committee** for the 3th ScienceOne Conference on Drug Discovery and Development (SCDDD2014) in Dubai, 21-23 January 2014
2014	**Reviewer** for the International Workshop on Chemical Science and Pharmaceutical Research (CSPR2014) Beijing 25-28 September
2014	**TPC member** of the International Conference on Pharmaceutical Sciences (ICPS2015) Dubai January 21-23, 2015
2015	**External Reviewer** of research proposals submitted to Croatian Science Foundation: Life & Sciences 2015
2015	**Member of Technical Program Committee** of the 2nd Int' Conference on Bioorganic and Medicinal Chemistry (ICBMC 2016).
2016	**Peer-reviewer** of Dove Medical Press journals: Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy; Drug Design, Development and Therapy; Research and Reports in Medicinal Chemistry
2016	**Editorial board Member** of The Open Medicinal Chemistry Journal
2016	**Reviewer** for VQR 2011-2014, Miur

2016 **Member of Academic committee** for the academics career progression (art 4. Regolamento di Ateneo,Università di Pisa) 2016
2016 **External Reviewer** of research proposal submitted to OPUS National Centre, Poland
2016 **Editorial Board Member** of Scientific Reports (Naturepublishing group)
2017 **Associate Editor** of Frontiers in Chemistry
2017 **Associate Editor** of Frontiers in Pharmacology –Section Anticancer drugs
2017 **Editor** of a Research topic in Frontiers in Chemistry entitled: Multi-target-directed ligands (MTDL) as challenging research tools in drug discovery: from design to pharmacological evaluation

Awards

2009 –**Farmindustria' Award**
Motivation: "For the outstanding results achieved in the development of new anti-ischemic mitochondrial ATP-sensitive potassium channels openers"
2011- **Young Researcher Award** (University)
Motivation: "Optimal scientific production estimated on 31/12/2010"
2011 – **Certificate of Appreciation** from ACS Publications
Motivation: "for the valuable contribution and dedicated service in the peer review of manuscript submitted to ACS Journals"
2013 – **Certificate of merit** – Special Committee (Pari Opportunità – Unipi)
Motivation: "For the outstanding results achieved in the research field."
2013- **Young Researcher Award** (University)
Motivation: "Optimal scientific production evaluated on 31/12/2011"
2016- **Speaker** at the "Open Day della Ricerca", annual event of meetings open to the public, dedicated to research.

INTERNATIONAL COLLABORATIONS

Hector DeLuca - University of Wisconsis (DeLuca)
Grazia Chiellini, Riccardo Zucchi - DIPINT- Universita di pisa
Marco Falasca- Curtin University, Perth (Australia)
Tania Maffucci -Blizard Institute (Falasca) London
Rongbiao Pi- Sun-yat sen University (China) (MAE)
Ana Paula Fonseca, Luis Carlos de Oliveira - Università de Coimbra (Lisbona)
Paola Parrella - IRCCS – Casa di sollievo e della sofferenza (Foggia)
Nicola Antonio Colabufo, Roberto Perrone - Università di Bari
Paola Fossa- Dipartimento di Farmacia Università di Genova
Raul R. Gainetdinov, Stefano Espinoza – Istituto Italiano di Tecnologia (IIT) Genova
Ettore Novellino – University of Naples
Luciana Marinelli- University of Naples Federico II
Ersoz Gonca – ZONGULDAK KARAELMAS Üniversity, Turkey

SCIENTIFIC ACTIVITY

The scientific activity of Prof. Rapposelli has allowed her to gain extensive experience in several experimental fields, such as medicinal chemistry and cardiovascular pharmacology; she is the author of more than 85 publications on peer-reviewed international scientific journals,11 international patents and more than 100 congress communications. The present rating of the citation index (H-index) is 22 (from the database Scopus).
The main currently research topics are:

- design and synthesis of new molecules targeting chemoresistance in cancer therapy
- Synthesis of new multitarget drugs through the combination of pharmacophoric moieties for the neurodegenerative diseases
- Synthesis of small molecules to treat GBM.

PATENTS

1. Balsamo, A.; Berardi, F.; Colabufo, N. A.; Perrone, R.; Rapposelli, S. *1-Phenylalkoxy-2β-phenylethyl derivatives as inhibitors of glycoprotein P (gp P) usable in cases of drug resistance*. IT2006RM0217A1, 2006
2. Balsamo, A.; Calderone, V.; Rapposelli, S.; Marchetti, P.; Torri, S. *Preparation of nitrooxy-substituted glibenclamide derivatives as hypoglycemic agents.* WO2008017925A2, 2008.
3. Balsamo, A.; Calderone, V.; Rapposelli, S. *Preparation of 4-spiroheterocyclic 2,2-dimethylchromanes as activators of ATP-sensitive potassium (KATP) channels*. WO2008007210A2, 2008.
4. Berardi, F.; Colabufo, N. A.; Perrone, R.; Balsamo, A.; Rapposelli, S.; Digiacomo, M. *1-Phenylalkoxy-2-β-phenylethyl derivatives as P-glycoprotein (P-GP) inhibitors useful in drug resistance events*. US20090093493A1, 2009..
5. Chiellini, G.; Rapposelli, S.; Zucchi, R. *Synthetic analogues of 3-iodothyronamine (t1am) and uses thereof*. WO2015151068A1, 2015.
6. Pi R.; Yang X. ; Rapposelli S. ; Chen Z. ; Wang S. ; Chu J. ; Tu Y. ; Liu P. ; Digiacomo M. ; Macchia M. *Rivastigmine-caffeic acid and rivastigmine-ferulic acid hybrids, their preparation and pharmaceutical compositions*. CN104860847 A, 2015
7. Sestito S.; Daniele, S.; Martini, C.; Rapposelli S.; Puricelli G. *COMPOSTI 2-OXO-1,2-DIIDROPIRIDIN-3-CARBOSSAMMIDE E LORO USO* COME *INIBITORI DI PDK1*. Italian Patent Filing 102015000022831. Filed 11 june 2015
8. Grassi F.; Lisignoli G.; Calderone V.; Rapposelli S. NEW MOLECULES FOR BONE TISSUE REGENERATION WO2016071863 (A1) 2016-05-12
9. RAPPOSELLI SIMONA [IT]; MARTINI CLAUDIA [IT]; CALDERONE VINCENZO [IT]; PURICELLI GUIDO [IT WO2016055454 (A1) - PHARMACEUTICAL COMBINATION FOR THE TREATMENT OF TUMORS
10. SESTITO Simona, DANIELE Simona, MARTINI Claudia, RAPPOSELLI Simona, PURICELLI Guido 2-OXO-1,2-DIHYDROPYRIDINE-3-CARBOXAMIDE 5 COMPOUNDS AND THEIR USE AS DUAL INHIBITORS OF PDK1/AurA" Italian deposit n° 102016000059838 10 june 2016. INTERNATIONAL SOCIETY FOR DRUG DEVELOPMENT S.R.L.
11. SESTITO Simona, DANIELE Simona, MARTINI Claudia, RAPPOSELLI Simona, PURICELLI Guido 2-OXO-1,2-DIHYDROPYRIDINE-3-CARBOXAMIDE COMPOUNDS AND THEIR USE AS INHIBITORS OF PDK1 PCT/EP2016/063293 10 june 2016

Sources of External Funding (Public and Private)

PUBLIC RESEARCH PROJECTS

PAST (From 2007-2011)

Grant Rapposelli (PI) 1/10/2007- 30/09/2008
Fondazione Cassa di risparmio Lucca
Development of new molecules for the treatment of myocardial ischemia
This research programme has the main objective in extending previous studies on the design, synthesis and pharmacological evaluation of new series of 4-spyroheterocyclic (6 or 5-

membered rings) benzopyranes which resulted endowed of cardioprotective activity. The study of the conformational restrictions and/or the nature of the substituents should allow to understand the most significant structure-activity relationships in this class of compounds and thus providing important indications about the interaction site of mito-KATP channel.
Role**: Principal Investigator**

Grant N°111S123 Ersoz Gonca (PI) 01/2010- 01/2011

TUBITAK NATIONAL PROJECT 2010
The effect of a new spiro-cyclic benzopyran activator of mitoKATP channels on ischemia reperfusion induced arrhythmias" – research activity in cooperation with ZONGULDAK KARAELMAS Üniversity (Turkey)
Role: **Partecipant**

20097FJHPZ_003 Perrone R.(National PI) 17/10/2011-17/10/2013
Research Projects of National Interest (PRIN)
Design and synthesis of new arylethylphenyl-derivatives as P-gp modulators for the treatment of neurodegenerative diseases and/or cerebral tumours.
The main objective of the project is to develop of new molecules able to circumvent or to limit the multidrug resistance related to the overexpression of P-gp in order to improve the already existing therapies for Alzheimer's disease and to ameliorate cognition and neuroprotection
Role: **Unit Principal Investigator**

PRESENT & RECENT

RBFR10ZJQT Marinelli L. (National PI) 08/03/2012-08/03/2015
Futuro in Ricerca (MIUR)- Settore ERC- LS - Life Sciences
Mitochondrial Medicinal Chemistry Against Cell Death-Resistant Cancers.
The main objective of the project is to generate and identify small molecules, using iterative design and synthesis, able to modulate the mitochondrial function in chemo-resistant tumors cells through the activation of effectors (i.e.MOMP) involved in the apoptosis processes
Role: **Unit Principal Investigator**

CN13MO9 Macchia M (National PI) 01/01/2013-01/01/2015
Ministero Affari Esteri (MAE)- Areas Biotechnologies and Medicines – Executive Programme of Scientific and Technological Cooperation between the Government of the Italian Republic and the Government of the People's Republic of China for the years 2013-2015.
Development of Novel Multi-target drug candidates against Alzheimer's Disease
The main objective of the project is to generate and identify new multitarget anti-AD drug with self-owned intellectual property rights. The project is closely bound up with the key health problem in China and Italy. The collaboration will be benefit to the develop new synthetic processes and also to implement the efficiency of well-known strategies by the use of strong points to overcoming weaknesses in professional technology as well as making up for the deficiency of research fund respectively.
Role: **Partecipant**

PRA2016_59 Da Settimo Federico (PI) 01/10/2015 – 01/11/2016
University of Pisa.
Development of nitrogenous heterocyclic derivatives as modulators of cell life / death processes

The main objective of the project is to design and synthesise new nitrogen-containing heterocycles compounds endowed of biological activity as potential anticancer drugs and/or as citoprotective agents.
Role: **Partecipant**

PRA2018_20 Rossello Armando (PI) 09/07/2018 – 08/07/2020
University of Pisa.
Target / Multitarget approaches for the design and development of Small Molecules for innovative therapies
The main objective of the project is to design and synthesise new small molecules following a multitarget approach for the development of anticancer drugs.
Role: **Partecipant**

PREVAGE Rapposelli Simona (PI) 06/2018-06/2020
Development of new potential drugs for the prevention of cellular aging and neurodegenerative diseases
Growing evidence reveal the existence of a close correlation between the progressive decline of normal cellular functions, increased oxidative stress (OS) and the reduction of the autophagic process. The main objective of this research is to develop new agents that reduce ROS toxicity and promote the removal of metabolic products accumulated in damaged cells. The combination of these two treatments, pro-autophagic and antioxidant, represents an attractive therapeutic strategy that could lead to effective pharmacological treatment both for the prevention of aging and for the treatment of neurodegenerative diseases, including Alzheimer's and the Parkinson's diseases
Role: **Principal Investigator**

PRIVATE RESEARCH PROJECTS

From1999 to 2003
Partecipant in research projects in the field of pharmaceutical research, funded by the following companies: **Angelini Ricerche S.p.A**.; **Chiesi Farmaceutici**; **Bracco S.p.A**.

From 2005 to 2007

Partecipant of a research project in the cardiovascular field, funded by the pharmaceutical company **Nicox S.p.a** through two consecutive annual research contracts with the Department of Pharmaceutical Science, University of Pisa

From 2013 to 2015
Scientific Director of a reseach project in the field of anticancer drugs and regenerative medicine, funded funded by the **International Society for Drug Development** (ISDD) (Milano,Italy) through two consecutive research contracts with Consorzio Interuniversitario Nazionale per la scienza e tecnologia dei materiali (INSTM)

From 2014 to 2015
Scientific Director of a research project focused on design and synthesis of anticancer drugs, funded by the **International Society for Drug Development** (ISDD) (Milano,Italy) through two consecutive research contracts with the Department of Pharmacy, of the University of Pisa.

From 2015 to 2016
Scientific Director of a Research project focused on the synthesis of new multitarget compounds for the treatment of multifactorial pathologies, funded by the **International Society for Drug Development** (ISDD) (Milano,Italy) through annual research contracts with the Department of Pharmacy, University of Pisa

From 2016 to 2017
Scientific Director of a Research project focused on the synthesis of new multitarget compounds for the treatment of neurodegenerative diseases, funded by the **International Society for Drug Development** (ISDD) (Milano,Italy) through annual research contracts with the Department of Pharmacy, University of Pisa

From 2017 to present
Scientific Director of a Research project focused on the synthesis of new multitarget compounds for the treatment of aggressive and unresponsiveness forms of cancer, funded by the **International Society for Drug Development** (ISDD) (Milano,Italy) through annual research contracts with the Department of Pharmacy, University of Pisa

Publications

1. Balsamo, A.; Cercignani, G.; Gentili, D.; Lapucci, A.; Macchia, M.; Orlandini, E.; Rapposelli, S.; Rossello, A. (2001) *Synthesis and inhibitory activity towards human leukocyte elastase of new 7α -methoxy and 7α -chloro(2-acyloxymethyl)cephem derivatives.* Eur. J. Med. Chem., **36**(2), 185-193.

2. Balsamo, A.; Bertini, S.; Gervasi, G.; Lapucci, A.; Nencetti, S.; Orlandini, E.; Rapposelli, S.; Rossello, A.; Soldani, G. (2001) *Enantiopure 3-(arylmethylidene)aminoxy-2-methylpropionic acids: synthesis and antiinflammatory properties.* Eur. J. Med. Chem., **36**(10), 799-807.

3. Balsamo, A.; Coletta, I.; Domiano, P.; Guglielmotti, A.; Landolfi, C.; Mancini, F.; Milanese, C.; Orlandini, E.; Rapposelli, S.; Pinza, M.; Macchia, B. (2002) *(E)-[2-(4-Methylsulphonylphenyl)-1-cyclopentenyl-1-methyliden](arylmethyloxy)amines. Methyleneaminoxymethyl (MAOM) analogues of diarylcyclopentenyl cyclooxygenase-2 inhibitors: synthesis and biological properties.* Eur. J. Med. Chem., **37**(5), 391-398.

4. Balsamo, A.; Coletta, I.; Guglielmotti, A.; Landolfi, C.; Lapucci, A.; Mancini, F.; Milanese, C.; Minutolo, F.; Orlandini, E.; Ortore, G.; Pinza, M.; Rapposelli, S. (2002) *Aryl-substituted methyleneaminoxymethyl (MAOM) analogues of diarylcyclopentenyl cyclooxygenase-2 inhibitors: effects of some structural modifications on their biological properties.* Eur. J. Med. Chem., **37**(7), 585-594.

5. Rossello, A.; Bertini, S.; Lapucci, A.; Macchia, M.; Martinelli, A.; Rapposelli, S.; Herreros, E.; Macchia, B. (2002) *Synthesis, Antifungal Activity, and Molecular Modeling Studies of New Inverted Oxime Ethers of Oxiconazole.* J. Med. Chem. , **45**(22), 4903-4912.

6. Macchia, M.; Antonello, M.; Bertini, S.; Di Bussolo, V.; Fogli, S.; Giovannetti, E.; Minutolo, F.; Rapposelli, S.; Danesi, R. (2003) *Conformationally restrained ceramide analogues: effects of lipophilic modifications on the antiproliferative activity.* Farmaco, **58**(1), 85-89.

7. Balsamo, A.; Coletta, I.; Guglielmotti, A.; Landolfi, C.; Mancini, F.; Martinelli, A.; Milanese, C.; Minutolo, F.; Nencetti, S.; Orlandini, E.; Pinza, M.; Rapposelli, S.; Rossello, A. (2003) *Synthesis of heteroaromatic analogs of (2-aryl-1-cyclopentenyl-1-alkylidene) (arylmethyloxy)amine COX-2 inhibitors: effects on the inhibitory activity of the replacement of the cyclopentene central core with pyrazole, thiophene or isoxazole ring.* Eur. J. Med. Chem., **38**(2), 157-168.

8. Macchia, M.; Bertini, S.; Fogli, S.; Giovannetti, E.; Minutolo, F.; Rapposelli, S.; Danesi, R. (2003) *Ceramide analogues in apoptosis: a new strategy for anticancer drug development.* Farmaco , **58**(3), 205-211.

9. Minutolo, F.; Antonello, M.; Bertini, S.; Rapposelli, S.; Rossello, A.; Sheng, S.; Carlson, K. E.; Katzenellenbogen, J. A.; Macchia, M. (2003) *Synthesis, binding affinity, and transcriptional activity of hydroxy- and methoxy-Substituted 3,4-Diarylsalicylaldoximes on estrogen receptors α and β.* Bioorg. Med. Chem. **11**(7), 1247-1257.

10. Minutolo, F.; Antonello, M.; Bertini, S.; Ortore, G.; Placanica, G.; Rapposelli, S.; Sheng, S.; Carlson, K. E.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A.; Macchia, M. (2003) *Novel Estrogen Receptor Ligands Based on an Anthranylaldoxime Structure: Role of the Phenol-Type Pseudocycle in the Binding Process.* J. Med. Chem. , **46**(19), 4032-4042.

11. Balsamo, A.; Mancini, F.; Milanese, C.; Orlandini, E.; Ortore, G.; Pinza, M.; Rapposelli, S.; Rossello, A. (2003) *Synthesis and prostaglandin synthase inhibitory activity of new aromatic O-alkyloxime ethers substituted with methylsulfonamido or methylsulfonyl groups on their aliphatic portion.* Farmaco , **58**(9), 707-714.

12. Minutolo, F.; Bertini, S.; Betti, L.; Di Bussolo, V.; Giannaccini, G.; Placanica, G.; Rapposelli, S.; Spielmann, H. P.; Macchia, M. (2003) *Synthesis of aniline-type analogues of farnesyl diphosphate and their biological assays for prenyl protein transferase inhibitory activity.* Farmaco, **58**(12), 1277-1281.

13. Minutolo, F.; Bertini, S.; Betti, L.; Danesi, R.; Gervasi, G.; Giannaccini, G.; Papi, C.; Placanica, G.; Barontini, S.; Rapposelli, S.; Macchia, M. (2003) *Stable analogs of geranylgeranyl diphosphate possessing improved geranylgeranyl versus farnesyl protein transferase inhibitory selectivity.* Bioorg. Med. Chem. Lett., **13**(24), 4405-4408.

14. Rapposelli, S.; Lapucci, A.; Minutolo, F.; Orlandini, E.; Ortore, G.; Pinza, M.; Balsamo, A. (2004) *Synthesis and COX-2 inhibitory properties of N-phenyl- and N-benzyl-substituted amides of 2-(4-methylsulfonylphenyl)cyclopent-1-ene-1-carboxylic acid and of their pyrazole, thiophene and isoxazole analogs.* Farmaco, **59**(1), 25-31.

15. Rossello, A.; Nuti, E.; Orlandini, E.; Carelli, P.; Rapposelli, S.; Macchia, M.; Minutolo, F.; Carbonaro, L.; Albini, A.; Benelli, R.; Cercignani, G.; Murphy, G.; Balsamo, A. (2004) *New N-arylsulfonyl-N-alkoxyaminoacetohydroxamic acids as selective inhibitors of gelatinase A (MMP-2).* Bioorg. Med. Chem., **12**(9), 2441-2450.

16. Minutolo, F.; Antonello, M.; Bertini, S.; Placanica, G.; Rapposelli, S.; Carlson, K. E.; Katzenellenbogen, J. A.; Macchia, M. (2004) *Diaryl-substituted salicyl- and anthranyl-ketoximes as potential estrogen receptor ligands.* Farmaco, **59**(8), 601-607.

17. Rossello, A.; Orlandini, E.; Nuti, E.; Rapposelli, S.; Macchia, M.; Di Modugno, E.; Balsamo, A. (2004) *Synthesis and antimicrobial activity of new 7β-(benzo[a]dihydrocarbazolyloxyacetyl)-substituted cephalosporins.* Farmaco, **59**(9), 691-696.

18. Breschi, M.C.; Calderone, V.; Digiacomo, M.; Martelli, A.; Martinotti, E.; Minutolo, F.; Rapposelli, S.; Balsamo, A. (2004) *NO-Sartans: A New Class of Pharmacodynamic Hybrids as Cardiovascular Drugs.* J. Med. Chem., **47**(23), 5597-5600.

19. Minutolo, F.; Asso, V.; Bertini, S.; Betti, L.; Gervasi, G.; Ghilardi, E.; Giannaccini, G.; Placanica, G.; Prota, G.; Rapposelli, S.; Macchia, M. (2004) *Stable propylphosphonic acid analogues of geranylgeranyl diphosphate possessing inhibitory activity on geranylgeranyl protein transferase.* Farmaco, **59**(11), 857-861.

20. Minutolo, F.; Antonello, M.; Barontini, S.; Bertini, S.; Betti, L.; Danesi, R.; Gervasi, G.; Giannaccini, G.; Papi, C.; Placanica, G.; Rapposelli, S.; Macchia, M. *Phosphonomethylphosphorylmethyl(oxy)-analogues of geranylgeranyl diphosphate as stable and selective geranylgeranyl protein transferase inhibitors.* Farmaco, **59**(11), 887-892.

21. Rossello, A.; Nuti, E.; Catalani, M.P.; Carelli, P.; Orlandini, E.; Rapposelli, S.; Tuccinardi, T.; Atkinson, S. J.; Murphy, G.; Balsamo, A. (2005) *A new development of matrix metalloproteinase inhibitors: twin hydroxamic acids as potent inhibitors of MMPs.* Bioorg. Med. Chem. Lett., **15**(9), 2311-2314.

22. Minutolo, F.; Asso, V.; Bertini, S.; Betti, L.; Ciriaco, M.; Danesi, R.; Gervasi, G.; Ghilardi, E.; Giovanetti, E.; Giannaccini, G.; Placanica, G.; Prota, G.; Rapposelli, S.; Macchia, M. (2005) *Variously substituted (phosphonoacetamido)oxy analogues of geranylgeranyl diphosphate (GGdP) as GGdP-transferase (GGTase) inhibitors and antiproliferative agents.* Med. Chem. , **1**(3), 239-244.

23. Minutolo, F.; Sala, G.; Bagnacani, A.; Bertini, S.; Carboni, I.; Placanica, G.; Prota, G.; Rapposelli, S.; Sacchi, N.; Macchia, M.; Ghidoni, R. (2005) *Synthesis of a Resveratrol Analogue with High Ceramide-Mediated Proapoptotic Activity on Human Breast Cancer Cells.* J.Med. Chem. , **48**(22), 6783-6786.

24. Minutolo, F.; Bertini, S.; Betti, L.; Danesi, R.; Gervasi, G.; Giannaccini, G.; Martinelli, A.; Papini, A.M.; Peroni, E.; Placanica, G.; Rapposelli, S.; Tuccinardi, T.; Macchia, M. (2006) *Synthesis of stable analogues of geranylgeranyl diphosphate possessing a (Z,E,E)-geranylgeranyl side chain, docking analysis, and biological assays for prenyl protein transferase inhibition.* ChemMedChem, **1**(2), 218-224.

25. Martelli, A.; Rapposelli, S.; Calderone, V. (2006) *NO-releasing hybrids of cardiovascular drugs.* Curr. Med. Chem., **13**(6), 609-625.

26. Breschi, M. C.; Calderone, V.; Digiacomo, M.; Macchia, M.; Martelli, A.; Martinotti, E.; Minutolo, F.; Rapposelli, S.; Rossello, A.; Testai, L.; Balsamo, A. (2006) *New NO-Releasing Pharmacodynamic Hybrids of Losartan and Its Active Metabolite: Design, Synthesis, and Biopharmacological Properties.* J. Med. Chem., **49**(8), 2628-2639.

27. Tuccinardi, T.; Calderone, V.; Rapposelli, S.; Martinelli, A. (2006) *Proposal of a New Binding Orientation for Non-Peptide AT1 Antagonists: Homology Modeling, Docking and Three-Dimensional Quantitative Structure-Activity Relationship Analysis.* J. Med. Chem., **49**(14), 4305-4316.

28. Tuccinardi, T.; Bertini, S.; Martinelli, A.; Minutolo, F.; Ortore, G.; Placanica, G.; Prota, G.; Rapposelli, S.; Carlson, K. E.; Katzenellenbogen, J. A.; Macchia, M. (2006) *Synthesis of Anthranylaldoxime Derivatives as Estrogen Receptor Ligands and Computational Prediction of Binding Modes.* J. Med. Chem., **49**(16), 5001-5012.

29. Minutolo, F.; Bertini, S.; Martinelli, A.; Ortore, G.; Placanica, G.; Prota, G.; Rapposelli, S.; Tuccinardi, T.; Sheng, S.; Carlson, K. E.; Katzenellenbogen, B. S.; Katzenellenbogen, J. A.; Macchia, M. (2006) *Salicylaldoximes and anthranylaldoximes as alternatives to*

phenol-based estrogen receptor ligands. ARKIVOC (Gainesville, FL, United States), **8**, 83-94.

30. Colabufo, Nicola A.; Berardi, F.; Perrone, R.; Rapposelli, S.; Digiacomo, M.; Balsamo, A. (2006) *Arylmethyloxyphenyl Derivatives: Small Molecules Displaying P-Glycoprotein Inhibition.* J. Med. Chem. , **49**(22), 6607-6613.

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