

# Giovanni SORBA

Professore ordinario  
CHIM/08 Chimica farmaceutica

Facoltà di Farmacia  
Dipartimento di Scienze Chimiche alimentari farmaceutiche e farmacologiche  
Tel.: 0321 375 750 Fax: 0321 375 271  
E-mail: sorba@pharm.unipmn.it

**CARRIERA ACCADEMICA:** 1999-2001: Professore associato confermato; 2001-2004: Professore straordinario; 2004-: Professore ordinario; 2009- Direttore DISCAFF.

**INSEGNAMENTI.** 1998-2001: Analisi dei farmaci II, Chimica Farmaceutica e Tossicologica I, PESF; 2001 – 2002 : Chimica Farmaceutica e Tossicologica I, Laboratorio di esercitazioni, Biotecnologie Farmaceutiche, 2002 – 2003 : Chimica Farmaceutica e Tossicologica I, Laboratorio di esercitazioni , Chimica Farmaceutica; 2003 – 2004 : Chimica Farmaceutica e Tossicologica I, Chimica Farmaceutica e Tossicologica II, Chimica Farmaceutica, Analisi chimico – tossicologica; 2004 – 2005 :Chimica Farmaceutica e Tossicologica I, Chimica tossicologica, Analisi chimico – tossicologica, chimica farmaceutica.

**CURRICULUM.** Laureato in Chimica e Tecnologia Farmaceutiche (110 con lode); ricercatore presso la Facoltà di Farmacia dell’Università di Torino per il gruppo CHIM 08 Chimica Farmaceutica dal 1983 al 1998; vincitore (1989) di una borsa di studio CNR per l’estero della durata di 6 mesi trascorso presso i laboratori diretti dal Prof. C.R. Ganellin all’University College di Londra. Professore Associato presso la Facoltà di Farmacia dell’Università del Piemonte Orientale per il gruppo CHIM 08 Chimica Farmaceutica dal 1998 al 2001; professore Ordinario presso la Facoltà di Farmacia dell’Università del Piemonte Orientale per il gruppo CHIM 08 Chimica Farmaceutica dal 2001.

**CAMPPI DI INDAGINE NELLA RICERCA.** Progettazione, sintesi, determinazione della struttura e dell’attività biologica di nuove NCE.

## TEMI CORRENTI DI RICERCA.

**Antitumorali.** Combretastatin A-4 is an antitumoral and antitubulin agent that is active only in its cis configuration. We have synthesized cis-locked combretastatins embodying a furazan ring (combretafurazans). To achieve this, we have developed a new strategy that exploits the dehydration of vicinal dioximes using the Mitsunobu reaction. Among the advantages of following such a strategy are the mild conditions used for the construction of the diarylfurazan derivatives, allowing for the presence of highly functionalized substrates and deactivated aromatic rings. Combretafurazans are more potent in vitro cytotoxic compounds compared to combretastatins in neuroblastoma cells, yet maintaining similar structure-activity relationship and pharmacodynamic profiles.

**NAADP.** Nicotinic acid adenine dinucleotide phosphate (NAADP) has been shown to be an intracellular Ca<sup>2+</sup>-releasing messenger in a wide variety of systems to date. Its actions are both potent and highly specific despite differing structurally from the endogenous cellular co-factor and its precursor, NADP, only in the substitution of a hydroxyl for the amine group at the 3' position of the pyridine ring. This substitution allows NAADP to bind to a membrane-localized binding site in sea urchin egg homogenates with an IC<sub>50</sub> at least 1000-fold greater than that of NADP as measured by competition radioligand binding assays. This suggests that the NAADP receptor protein must include certain features in the NAADP binding site that regulate this specificity. In order to investigate this interaction, we synthesised a series of NAADP analogues differing from NAADP at the 3' position of the pyridine ring that included both simple carboxylic acid analogues as well as a series of isosters. We then investigated both their affinity for the NAADP binding site in sea urchin egg homogenates and their ability to activate the NAADP sensitive Ca<sup>2+</sup> channel. We hereby show that a negative charge at the 3' position is an important determinant of affinity but the protein displays a large tolerance for the size of the group. Furthermore, the protein does not easily accommodate multiple charged groups or large uncharged groups.

## PUBBLICAZIONI PIÙ RECENTI.

GROLLA A.A, PODESTÀ V, CHINI M.G, DI MICCO S, VALLARIO A, GENAZZANI A.A, CANONICO P.L, BIFULCO G, TRON G.C, SORBA G., PIRALI T (2009). Synthesis, biological evaluation, and molecular docking of Ugi products containing a zinc-chelating moiety as novel inhibitors of histone deacetylases. JOURNAL OF MEDICINAL CHEMISTRY, vol. 52; p. 2776-2785.

CAFICI L, PIRALI T, CONDORELLI F, DEL GROSSO E, MASSAROTTI A, SORBA G., CANONICO P.L, TRON G.C, GENAZZANI A.A (2008). Solution-phase parallel synthesis and biological evaluation of combretatriazoles. JOURNAL OF COMBINATORIAL CHEMISTRY, vol. 10; p. 732-740.

GALLI U, ERCOLANO E, CARRARO L, BLASI ROMAN C.R, SORBA G., CANONICO P.L, GENAZZANI A.A, TRON G.C, BILLINGTON R.A (2008). Synthesis and biological evaluation of isosteric analogues of FK866, an inhibitor of NAD salvage. CHEMBIOCHEM, vol. 3; p. 771-779.

PIRALI T, PAGLIAI F, MERCURIO C, BOGGIO R, CANONICO P.L, SORBA G., TRON G.C, GENAZZANI A.A (2008). Triazole-modified histone deacetylase inhibitors as a rapid route to drug discovery. JOURNAL OF COMBINATORIAL CHEMISTRY, vol. 10; p. 624-627.

TRON G.C, PIRALI T, BILLINGTON R, CANONICO P.L, SORBA G., GENAZZANI A (2008). Click chemistry reactions in medicinal chemistry: applications of the 1,3-dipolar cycloaddition between azides and alkynes. MEDICINAL RESEARCH REVIEWS, vol. 28; p. 278-308.

GALLI U, OLIARO-BOSO S, TARAMINO S, VENEGONI S, PASTORE E, TRON GC, BALLIANO G, VIOLA F, SORBA G. (2007). Design, synthesis and biological evaluation of new (2E,6E)-10-(dimethylamino)-3,7-dimetil-2,6-decadien-1-ol ethers as inhibitors of human and Trypanosoma cruzi oxidosqualene cyclase. *BIOORGANIC & MEDICINAL CHEMISTRY LETTERS*, vol. 17; p. 220-224.

IMPERIO D, PIRALY T, GALLI U, PAGLIAI F, CAFICI L, CANONICO PL, SORBA G., GENAZZANI A.A, TRON G (2007). Replacement of the Lactone moiety on podophyllotoxin and steganacin analogues with a 1,5-disubstituted 1,2,3-triazole via rutenium-catalyzed clik chemistry. *BIOORGANIC & MEDICINAL CHEMISTRY*, vol. 15; p. 6748-6757.

PIRALI T, GATTI S, DI BRISCO R, TACCHI S, ZANINETTI R, BRUNELLI E, MASSAROTTI A, SORBA G., CANONICO PL, MORO L, GENAZZANI A.A, TRON GC, BILLINGTON R.A (2007). Estrogenic Analogues Synthesized by Click Chemistry. *CHEMMEDCHEM*, vol. 1; p. 437-440.

PAGLIAI FRANCESCA, PIRALI TRACEY, DEL GROSSO ERIKA, DI BRISCO RICCARDO, TRON GIAN CESARE, SORBA G., GENAZZANI ARMANDO A. (2006). Rapid synthesis of triazole-modified resveratrol analogues via click chemistry. *JOURNAL OF MEDICINAL CHEMISTRY*, vol. 49; p. 467-470.

PIRALI T, BUSACCA S, BELTRAMI L, IMOVILLI D, PAGLIAI F, MIGLIO G, MASSAROTTI A, VEROTTA L, TRON GC, SORBA G., GENAZZANI AA (2006). Synthesis and cytotoxic evaluation of combretafurans, potential scaffolds for dual-action antitumoral agent. *JOURNAL OF MEDICINAL CHEMISTRY*, vol. 49; p. 5372-5376.

TRON GC, PIRALI T, SORBA G., BUSACCA S, GENAZZANI AA (2006). Medicinal Chemistry of Combratastatin A4: Present and future directions. *JOURNAL OF MEDICINAL CHEMISTRY*, vol. 49; p. 3033-3044.

*Orario di Ricevimento*

*Presso lo studio in largo Donegani 2,3.*

*In qualsiasi momento previo appuntamento concordato per posta elettronica.*