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CHEMISTRY ENABLING DRUG DISCOVERY

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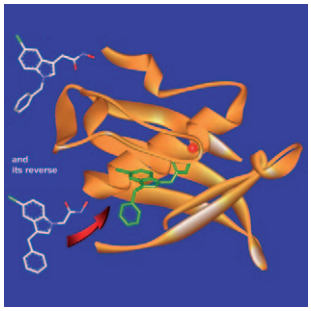
## COVER PICTURE



**The cover picture shows** a "reverse" indole derivative in complex with *Bacillus stearothermophilus* peptide deformylase (PDF). This compound was selected from a structure–activity relationship study as a potent inhibitor of bacterial PDFs and shows antibacterial activity toward *Bacillus subtilis* as well as other pathogens such as *Streptococcus pneumoniae* and *Staphylococcus aureus*. For more details, see the Full Paper by I. Artaud et al. on p. 261 ff.

## NEWS



## REVIEWS

**ChemMedChem succeeds IL FARMACO, a journal of the Società Chimica Italiana**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Further masthead information follows directly after the Table of Contents.

## CONCEPTS



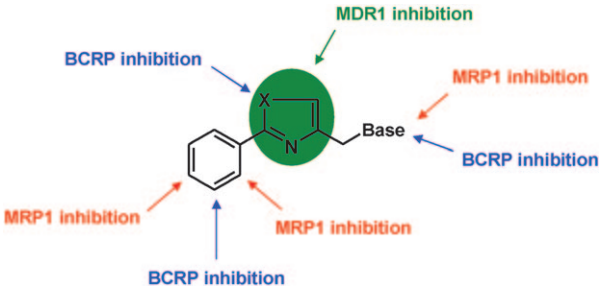
## COMMUNICATIONS



## FULL PAPERS

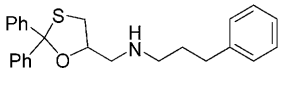




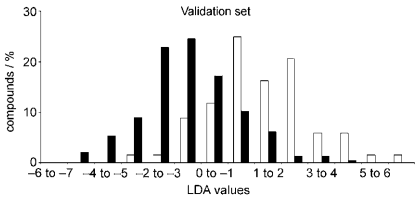

**The 2-aryloxazole and 2-arylthiazole** scaffolds were used for generating compounds that we characterized for their inhibitory activity toward ATP binding cassette transporters involved in multidrug resistance, such as BCRP and MRP1, by using tumor cell lines overexpressing each transporter. These SAR studies are a significant step toward improving the inhibitory potency against P-glycoprotein, BCRP, and MRP1.





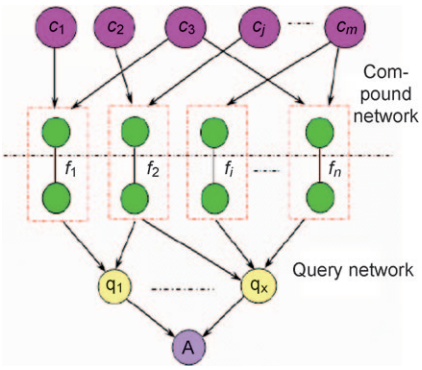

**A selective 5-HT$_{1A}$ receptor agonist**: A new series of ligands acting at 5-HT$_{1A}$ serotonin receptor were identified. Among them (2,2-diphenyl-[1,3]oxathiolan-5-yl-methyl)-(3-phenyl-propyl)amine (shown) possesses outstanding activity (p$K_i$ = 8.72, pD$_2$ = 7.67, $E_{max}$ = 85) and selectivity (5-HT$_{1A}$/$\alpha_{1D}$ > 150), and represents a new 5-HT$_{1A}$ agonist chemotype.





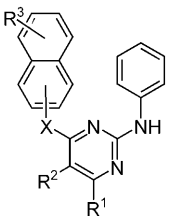

**A QSAR model** for the prediction of CNS activity was developed and validated based on data from an in-house database of "drug-like" compounds. The model has demonstrated its applicability for novel chemical structures and its usefulness for the design of CNS-focused compound libraries.






**An inference network model** for molecular similarity searching: The similarity search problem is modeled using inference or evidential reasoning under uncertainty. The inference network model treats similarity searching as an evidential reasoning process in which multiple sources of evidence about compounds and reference structures are combined to estimate resemblance probabilities.

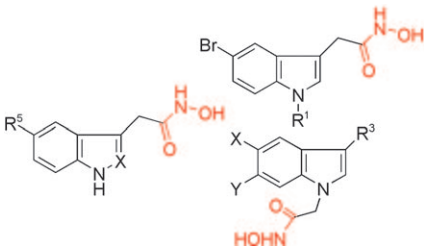





**A novel series** of diarylpyrimidine analogues (DAPYs) featuring a naphthyl moiety at the C4 position were designed, with all compounds exhibiting strong activity against wild-type HIV-1.

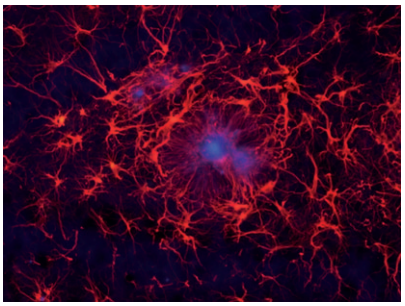
  



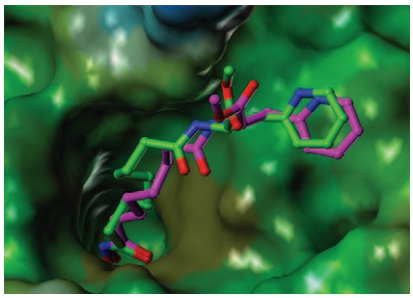

**SAR by NMR**: A series of indole compounds derived from 5-bromo-1*H*-indole-3-acetohydroxamic acid were synthesized. Their inhibitory activities were evaluated against purified peptide deformylases (PDFs), and their antibacterial activities against *B. subtilis*, *E. coli* (wild type and *tolC*), and a variety of pathogens were also determined. The potency of the best inhibitors was related to the NMR footprints of the respective acids with $^{15}$N-labeled *E. coli* Ni-PDF.





**Plaque visualisation**: We identified three different D-enantiomeric peptides that bind to Alzheimer's amyloid β (Aβ1-42). As there is currently no definitive pre-mortem diagnosis for Alzheimer's disease, we investigated the peptides' suitability as molecular probes for in vivo imaging in transgenic mouse models.





**Pyridylalanine inhibitors** of histone deacetylase (HDAC) have been synthesized that show selectivity for the isoform HDAC6 over HDAC1 in vitro. This selectivity was also identified in cancer cells by analyzing tubulin versus histone acetylation. The compounds show decreased intrinsic cytotoxicity relative to pan-HDAC inhibitors, but show antiproliferative synergy with the proteasome inhibitor bortezomib.

Supporting information on the WWW (see article for access details).

A video clip is available as Supporting Information on the WWW (see article for access details).

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## BOOKS



  

## SERVICE



**All the Tables of Contents may be found on the WWW under: http://www.chemmedchem.org**

**Issue 1, 2009, was published online on January 7, 2009.**

## CORRIGENDUM

*K.-S. Yeung,* N. A. Meanwell*

**Inhibition of hERG Channel Trafficking: An Under-Explored Mechanism for Drug-Induced QT Prolongation**

*ChemMedChem* **2008**, *3*, 1501–1502

DOI 10.1002/cmdc.200800170

The first sentence, "Functional blockage of the human *ether-á-go-go-related gene* (hERG or KCNH2) encoded cardiac potassium channel is responsible for the rapidly activating component of the delayed rectifier $K^+$ current ($I_{kr}$), which can delay ventricular cell repolarization." should read "The human *ether-á-go-go-related gene* (hERG or KCNH2) encoded cardiac potassium channel is responsible for the rapidly activating component of the delayed rectifier $K^+$ current ($I_{kr}$). Functional blockage the hERG channel can delay ventricular cell repolarization."



  